BUYING MEDICAL TECHNOLOGY IN THE DARK: HOW NATIONAL HEALTH REFORM CAN TURN ON THE LIGHTS AND PROMOTE TECHNOLOGY INNOVATION AND COST SAVINGS

HEARING

BEFORE THE

SUBCOMMITTEE ON REGULATION, BUSINESS OPPORTUNITIES, AND TECHNOLOGY

OF THE

COMMITTEE ON SMALL BUSINESS HOUSE OF REPRESENTATIVES

ONE HUNDRED THIRD CONGRESS

FIRST SESSION

WASHINGTON, DC, OCTOBER 21, 1993

Printed for the use of the Committee on Small Business

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BUYING MEDICAL TECHNOLOGY IN THE DARK: HOW NATIONAL HEALTH REFORM CAN TURN ON THE LIGHTS AND PROMOTE TECHNOLOGY INNOVATION AND COST SAVINGS

THURSDAY, OCTOBER 21, 1993

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON REGULATION, BUSINESS
OPPORTUNITIES, AND TECHNOLOGY,
COMMITTEE ON SMALL BUSINESS,
Washington, DC.

The subcommittee met, pursuant to notice, at 9:35 a.m., in room 2359–A, Rayburn House Office Building, Hon. Ron Wyden (chairman of the subcommittee) presiding.

Chairman WYDEN. The subcommittee will come to order. This year in America, health care costs will total approximately $900 billion. Each year this bill grows by $100 billion and technology is the largest single contributor to this massive growth in health expenditures. Many economists have estimated that 40 to 50 percent of the growth in health costs is attributable to new technologies.

Unfortunately, most medical technology is now being purchased in the dark. Americans can obtain detailed information about a breakfast cereal before they buy it, but our Nation's largest health buyers can rarely find good information comparing the merits of a new medical technology to currently available products.

As we will see this morning, this lack of comparative information permits questionable medical technologies to be widely used for years before their performance record catches up with them. This medical technology information gap has produced two problems.

First, patients can be needlessly harmed when safer technologies are replaced by inferior ones; and second, vast sums of money are wasted on costly technologies when others would accomplish the same result for less. Every single one of the major health reform proposals now before the Congress gives short shrift to the medical technology information gap.

Most of these proposals assume that somehow either the Government or the market is poised to buy smart if only the proper incentives are offered.

The fact is that no incentive to buy smart is going to do the job unless buyers have the basic essential information they need to know what to buy. What is needed is a concerted national campaign to discover the comparative effectiveness of medical tech-

nologies and feed a steady stream of this information to payers, practitioners, and patients across our country.

The fact is, it is time for the Federal Government to overhaul its approach to medical technology.

The centerpiece of a new strategy should be changes in Federal law that provide specific significant incentives for drug and device companies to, on a voluntary basis, perform clinical trials comparing their new technologies to existing ones and it should begin during premarket testing.

For many months now, opponents of health reform have been trying to sell the American public on the idea that they must choose between medical cost containment and access to lifesaving medical technologies. This is fear mongering built on false choices.

If national health reform makes it possible for health buyers and users to conveniently compare competing medical technologies, cost savings can be achieved while simultaneously improving the health of our citizens. The key is to get information out to prospective technology buyers early before money and lives are wasted.

Through a new strategy for purchasing medical technology, health reform can serve as a trampoline for medical innovation and help find new cures for dreaded disease, while still saving money through the elimination of waste and inefficiency.

The subcommittee has compiled a set of case studies that exemplify our inability to purchase and use medical technology wisely. Each of these supposedly new and improved technologies was marketed to doctors, patients, and payers as a significant advance over existing drug or device technologies.

In case study number one, balloon angioplasty is unsuccessful in unclogging coronary arteries in up to a third of the patients. An alternative procedure called an atherectomy has become popular which involves boring out and opening up clogged coronary arteries with a tiny whirling drill.

This year, after 50,000 patients have already undergone this procedure, atherectomy was found to be no more effective, less safe, and significantly more expensive than balloon angioplasty.

In case study number two, urinary tract infections are the most common hospital acquired infection. A silver impregnated latex urinary catheter was sold for years at four times the price of plain latex catheters on the strength of the claim that it would reduce urinary tract infection, but when a large clinical trial was finally done comparing the performance of the two catheters, the high price silver-coated catheter was found to produce, in fact, more infections in a larger proportion of catheterized patients.

In case number three, heart patients who were prone to abnormal heart rhythms or arrythmia are at a higher risk of sudden death. Several drugs were marketed for treatment of these patients because the drugs could suppress abnormal heart rhythm, but after years of widespread use, the National Institutes of Health found patients using the drugs were actually at greater risk of sudden death than those that were using the placebo.

Research published this month confirms the best treatment for this problem remains a class of older inexpensive drugs used for high blood pressure.

In case study number four, for at least the last decade, standard therapy for stomach or intestinal ulcers has been treatment with a class of expensive drugs called H2 and Tagament. The Medicaid program spends more on this group of drugs than for any other, amounting to almost 10 percent of all drug spending for the poor.

Over the past several years, mounting evidence has established that most of these ulcers are caused by a bacterium that can be more effectively treated with an inexpensive combination of two off-patent antibiotics and Pepto-Bismol.

In case study five, adult respiratory distress syndrome attacks the lungs of some 15,000 young Americans each year, killing more than half of them. One high-technology device used to keep these patients alive until their lungs cleared up involved circulating the patient's blood through machines to add oxygen and remove the wastes.

When researchers compared this latest technology to making better use of their existing hospital ventilator equipment, they achieved significantly better survival rates and saved about $40,000 per patient.

These studies can teach us several lessons about the current state of the art of American health care. First, the true cost of widespread use of poorly understood drug and device technologies far exceeds the cost to the health care system of these products. The urinary catheter that causes urinary tract infections may cost $20, but result in thousands of dollars in hospitalization costs.

Similarly, an MRI machine may cost $500,000 but account for many millions in billings during its useful life.

Lesson two, there is obviously much more art than science in everyday medicine. Medical intervention for the firm scientific foundation are the exception rather than the rule. When comparative trials have been done, all too often they reveal that newer technologies are more expensive, offer no advantage over the existing technology, and may even be inferior in terms of safety and effectiveness.

Finally, safer, more effective, and less expensive medical technologies are being ignored for want of the aggressive corporate sponsorship and promotion needed in today's system to bring them to the attention of physicians.

With these lessons in mind, I would like to propose that targeted voluntary incentives be enacted into law to encourage innovation and bridge the medical technology information gap. The first such incentive would provide for extended exclusivity for comparative study. Companies that conduct one or more clinical studies comparing their new drug or device product to a product already used for the same indication could receive extended exclusivity of 3 years for the first such study with FDA authorized to grant additional single-year increments for more or particularly large scale clinical studies.

I would like to emphasize that for medical devices, extended exclusivity would apply to patented features of the device, not the entire device nor its functional attributes. I believe that this feature is important to reassure those in the industry who are concerned that exclusivity should serve as a reward and not an impediment to steady incremental improvements with the technology.

Incentive number two would provide for extended exclusivity for special population study. Companies who conduct one or more clinical studies analyzing the effectiveness of a product, the geriatric, pediatric or at-risk minority population would receive extended exclusivity for 2 years duration if the study is completed in time for results to be incorporated into initial product labeling, and also 1 year's duration would be available if the study is completed and supplemental labeling is approved prior to expiration of any other exclusivity enjoyed by the product.

Before such a study could qualify a product for extended exclusivity, FDA approval of the study design would be necessary. FDA's judgment would have to be rendered within 60 days of submission of the study designed to the agency for review and approval to ensure that those industries participating in this process would get a fast response from the Federal Government.

Incentive number three would provide for expedited approval for superior products. FDA would have 30 days after receiving the final results of an approved trial to determine whether the study establishes the product as a superior product. FDA may deem a product superior either for offering demonstrated clinical superiority for a defined population or by offering equivalent effectiveness while significantly reducing the cost of caring for a defined population.

If the FDA deems a product superior and the product has not yet been approved for marketing, the FDA would be obligated to give the product application priority over all but other products of similarly demonstrated superiority. If FDA approval for a product occurs more than 60 days after the agency has deemed the product superior, the manufacturer could receive an additional month of exclusivity for each additional month following expiration of the 60-day prior approval period.

Finally, and most importantly, there must be prompt dissemination of trial results. Sponsors of superior products will also benefit from active governmental dissemination of trial results to health plans and practitioner groups with the stipulation that the Government found the company's clinical study design met rigorous quality standards.

Results would be disseminated on an electronic bulletin board and through other means, and the Chair would like to note that this is exactly what is done, for example, in the physics area where physicists distribute information this way. This is what is being done in the environmental area to distribute information with respect to environmental issues, and it seems to me it is high time in this country that large buyers of health care, like HMO's and insurers, and also physicians and patients be in a position to get state of the art information about medical technology.

We look forward to receiving testimony this morning, particularly on this issue, because it is especially important that this information get out. Doctors, for example, who are harried medical professionals are in great need of current and reliable information, and we are anxious to get the input of the medical industry community as to the best way that this technology can get to physicians for use in their day-to-day decisionmaking.

This proposal adds legislative authority for two key elements that are necessarily missing from FDA Commissioner Kessler's recent constructive proposal to expedite medical device approvals for products that promise a significant therapeutic advantage.

First, this proposal provides the solid comparative clinical data necessary for the agency to distinguish real breakthrough technologies from some of the initial promising technological turkeys that we are going to hear about this morning.

Second, this proposal authorizes the FDA to expedite approval of products that reduce health costs while matching the competition on clinical effectiveness.

Finally, this proposal offers two other advantages missing from other medical technology assessment schemes suggested to date. First, it mobilizes the potential for significant private sector resources to pay for this vital research, without which this Nation will inevitably enter an era in which vigorous cost cutting will continue to be done in the dark.

The information generated under this proposal, unlike any other that is now before the Congress, would become available early in the product life cycle when buyers, physicians, and patients need it the most.

Based on my discussions with individual firms and representatives of the manufacturers, I believe this approach offers benefits for manufacturers of drugs and devices as well as the rest of the stakeholders in the American health system.

I respect the preference of major drug and device associations not to send representatives to testify at this morning's hearing, but I wish to emphasize to them that we will be consulting very closely with them and their individual members to ensure their active participation as this proposal that is discussed today is further refined.

I also intend to pursue this as a member of the health committee chaired by subcommittee Chairman Waxman and full committee Chairman Dingell when the national health reform legislation is sent to the Energy and Commerce Committee.

It seems to me that the Congress has a choice: Build national health reform on a solid scientific foundation, or pretend that reform can be constructed on a shaky, technological base. We are going to try to fill the medical technology information gap and secure a bright future for national health reform.

I want to thank in particular our Ranking Minority Member, the gentleman from Texas, who on all matters has worked in a bipartisan way and certainly there isn't a shred about the medical technology discussion issue which is partisan.

I look forward to working with my friend and colleague, Mr. Combest.

Mr. COMBEST. Thank you, Mr. Chairman.

Mr. Chairman, today's hearing about improving medical information so that doctors and patients can make more knowledgeable and efficient health care choices is important.

Witnesses here today will discuss how they feel the current system is lacking in providing incentives for industry to complete comparative studies between medical products.

In preparing for this hearing, it has become crystal clear that, like health care reform in general, the problems we are asked to

discuss are highly complex. It appears that although Members may be seeking the same endpoints, how they arrive at the prize will significantly differ.

I support efforts to expedite FDA review of drugs and devices. We need to help create an environment where Federal regulators are partners and not adversaries in health care technology. While in Europe, it may take only 25 government regulatory officials to approve a medical device, it can take more than 260 full-time officials at the FDA.

The health care device and drug industries are two of the Nation's true success stories, for the United States clearly and unquestionably leads the world in finding lifesaving products. Whatever this subcommittee or Congress decides to do on this issue or health care reform, we must not compromise the ability of these entrepreneurs to compete and innovate.

I philosophically believe that increased competition is the key to bringing health care costs down. I discussed the issues of comparative studies and outcome research within the device industry with doctors and hospital administrators in my district. They told me more should be done, but that under today's increasing cost pressures, they were making tough decisions and making them in the light of day.

They said in Texas where there is no cap on medical liability, we make sure that we have sound information on the safety and effectiveness of drugs and devices. They also said when a salesman calls on them, if they do not trust or cannot verify clear treatment, improvements, or cost savings, they don't buy it.

Furthermore, I have major differences when it comes to those who will be the arbiter of new technologies. I do not want the Federal Government becoming a referee subjectively determining which device they feel is best for the health care treatment of my constituents.

I have much more faith in the health care professionals in my district than the bureaucrats in Washington.

Finally, Mr. Chairman, because it appears that small business will be tasked with paying for much of the President's health care reform, and while we won't hear from them today, I will be glad to work with you so that in the future, we may have hearings on their input from the small business sector.

I thank you for holding this hearing, Mr. Chairman.

[Mr. Combest's statement may be found in the appendix.]

Chairman WYDEN. I thank the gentleman and certainly look forward to pursuing these issues with him.

Gentleman from California, Mr. Kim.

Mr. KIM. No comments.

Chairman WYDEN. All right. Let us go right then directly to our witnesses. We want to welcome John Williamson, M.D., director, Regional Medical Education Center of the Veterans Administration Medical Center in Salt Lake City and Brent James, executive director of IHC Institute for Health Care Delivery Research.

Gentlemen, we welcome you. We thank you very much for coming a long way. It is the practice of this subcommittee to swear all the witnesses who come before us. Do either of you have any objec-

tion to being sworn as a witness? Please rise and raise your right hand.

(Witnesses sworn.)

Chairman WYDEN. Gentlemen, we are going to make your prepared statements a part of the hearing record in their entirety and we would like to ask you to summarize your principal views in 5 minutes. We are going to try a bipartisan refinement of our hearings today, bringing forward an actual egg timer after many years of trying to get our friendly witnesses to just speak with us, and I think that is really the challenge.

We will put your statements in the record in their entirety. We welcome both of you and let us begin with you, Dr. Williamson.

Mr. COMBEST. Mr. Chairman, if the timing process is truly bipartisan, don't you think the timer should be put between us?

Chairman WYDEN. I think that is a superb idea. Dr. Williamson.

TESTIMONY OF JOHN WILLIAMSON, M.D., DIRECTOR, REGIONAL MEDICAL EDUCATION CENTER, VETERANS ADMINISTRATION MEDICAL CENTER, SALT LAKE CITY, UTAH

Dr. WILLIAMSON. Mr. Chairman, distinguished members of the subcommittee, it is an honor and a pleasure to be asked to give testimony regarding the Chairman's important proposal.

I have been a physician and academic researcher for 30 years, working at Johns Hopkins, Harvard, and recently the University of Utah. I have specialized in health care quality assurance and health science information management, both directly involving medical technology assessment.

Most recently, I have been a member of the interagency task force for health care reform chaired by Hillary Rodham Clinton.

I and trusted colleagues I have contacted judge this proposal to be both urgent and critical. If implemented, it could make a major contribution in reducing health care costs and improving the quality of care. Generating valid comparative assessment data is difficult, and even when produced, its wide dissemination may take up to 10 or 15 years, as pointed out by Chalmers at Harvard.

In my testimony, I would like to suggest three provisions that might make this important proposal even stronger.

One, emphasize use of more extensive research guidelines to assure soundness of new information generated. Two, develop syntheses of existing studies to both strengthen new research and directly facilitate current purchasing. Three, use computerized expert systems to assure rapid dissemination and appropriate use of the above information that is generated.

My first suggestion is that there are clear advantages for encouraging manufacturers to generate new studies of efficacy, safety, and cost-effectiveness of the drugs and devices as compared with current alternatives. However, this effort could be strengthened by emphasizing the use of enhanced research safeguards that go beyond FDA approval of study design.

Renowned investigators as Mosteller at Harvard and Hillman at Pennsylvania suggest this. Hillman supports his need in terms of cost-effectiveness research by stating that pharmaceutic cost-effectiveness analyses sometimes tend to be marketing devices rather than sound clinical research.

Mills' New England Journal of Medicine article stated, "If you torture your data long enough, they will tell you whatever you want to hear." However, use of sound guidelines could substantially reduce bias and improve the value of the data produced.

My second suggestion is to stress that it is difficult to identify, validate, and synthesize results from either new or old technology assessments. However, new techniques now exist to alleviate this problem. I would suggest incentives and funding for researchers to produce validated information syntheses of information that now exists.

Current published reviews are often flawed for lack of an adequate strategy for searching new literature or lack of appropriate validation of the information included. Excellent narrative syntheses and statistical syntheses called med analyses are now available as models.

My third and final suggestion would be for incentives for funding to disseminate technology assessment findings by use of computerized expert systems. Haynes at McMasters University states, "Peer review journals impede the dissemination of validated advances."

When facing a patient, busy physicians will rarely read journal articles or even guidelines. Expert systems can apply the power of such technology assessments in milliseconds while the physician or purchaser is making his decision. Such resources are key to assuring timely and appropriate purchase and use of drugs and devices that are proven to be superior.

To illustrate, recently a 40-year-old male experiencing symptoms of a heart attack was admitted to a major cardiac center. Later that day, independent of professional care, the patient's initial findings were put into an expert system called Iliad which incorporates over 1,600 computerized guidelines.

The result indicated a low probability of a heart attack with a much higher probability of a esophageal spasm, easily treated by new proven pharmaceuticals. Ten weeks later, after a $12,000 work-up, including coronary catheterization, the diagnosis of esophageal spasm was finally made.

On the first day of the patient's illness, the expert system had suggested the correct diagnosis that could easily have been confirmed by the physician asking this patient of his history of stomach problems. This information might have averted hospitalization, inappropriate use of expensive potentially life-threatening devices, and appropriate use of recent proven new pharmaceuticals.

I will conclude with one final example about an expert system developed for patient use. A middle-aged male who recently had nausea and vomiting volunteered to use this computer system to elicit his own history while waiting for the doctor in the doctor's waiting room. The product was a printed history together with probabilities of the most likely diagnoses.

Unfortunately, clinicians usually disregard these printouts. The practitioner caring for this man diagnosed gastroenteritis and sent him home with a prescription. As the patient left, the clinician happened to glance at the expert system's findings. He yelled at the nurse to get the patient back for an emergency hospital admission.

The doctor had failed to ask the patient about the character of the vomitus. The expert system found that the vomitus had resem-

bled coffee grounds the day before and was bright red this morning. This patient was hemorrhaging from an ulcer. If drug treatment only had been given, the outcome might have been tragic.

I suggest to this subcommittee that incentives for use of more adequate research guidelines, together with incentives and funds for increasing production of valid literature syntheses and dissemination by computerized expert systems could have immediate and dramatic benefits on technology purchasing and use.

This excellent proposal augmented by these provisions could result in substantial cost savings and better health outcomes for the Nation. I thank you for this opportunity to share these ideas with you.

Chairman WYDEN. Doctor, thank you very much, and I very much appreciate all your interest and assistance on this and we will have some questions in just a moment.

[Dr. Williamson's statement may be found in the appendix.]

Chairman WYDEN. Dr. James, welcome. We will make your prepared remarks a part of the record and I understand that you are on a pretty tight time schedule, so we will begin the questioning with my colleagues and maybe we will start the questioning with you right after your statement and excuse you at that time.

Doctor, welcome.

TESTIMONY OF BRENT JAMES, M.D., EXECUTIVE DIRECTOR, IHC INSTITUTE FOR HEALTH CARE DELIVERY RESEARCH, SALT LAKE CITY, UTAH

Dr. JAMES. Thank you very much. Adult respiratory distress syndrome is a disease of the lungs that affects about 15,000 Americans each year. It is primarily a disease of young men and, in fact, across all cases, more than half of those young men die. For one particular subgroup, 80 to 90 percent die.

It is a very pernicious decease because if you can achieve a good outcome, they go on to lead full and normal lives and it affects the young.

A clinical trial conducted at LDS Hospital in Salt Lake City recently compared a new complicated high-technology therapy for adult respiratory distress syndrome called extra-corporeal CO_2 removal, or $ECCO_2$ R, to traditional ventilator management. The results of that trial are summarized on page four.

Fundamentally, $ECCO_2$ R achieved as it was marketed to achieve. In that group of patients who had about a 15 percent survival rate, it achieved about 40 percent survival. The interesting fact of the study discovered though was that traditional ventilator management, when managed carefully, actually achieved better survival than $ECCO_2$ R.

It also did it for a much lower cost, about $40,000 per case cheaper than this new high technology device.

This is but one of many studies that we have conducted within Intermountain Health Care of similar technologies, just in passing though to say that it doesn't begin to even scratch the surface of the technologies that could be studied.

I just wanted to emphasize a few points that we think that we have learned from those studies. The first is this: Only about 10 to 20 percent of what we do in health care delivery of common

medical practices has any basis whatsoever in scientific research. The rest is based upon experience and tradition.

Now, that doesn't necessarily mean that it is wrong. It just means that we don't know what is best and that physicians and other health care deliverers can hold legitimate differences of opinion about best care delivery.

As Dr. Williamson has pointed out, that is exacerbated by the slow diffusion of scientific knowledge from the literature into practice. More than that, he has also pointed out that the very complexity of the system makes it very difficult for physicians to synthesize and make decisions about medical technologies or treatment decisions and choices in a clinical setting.

Those taken together is the primary basis for the high rate of variation that we see in clinical care delivery today in America. David Eddy and Jack Wennberg have summarized that as professional uncertainty.

There is some controversy about the benefits of eliminating that variation in medical practice, but particularly we think that it may have three advantages. When you eliminate variation, we believe that medical outcomes often improve. It was shown in our adult respiratory distress syndrome case.

We believe that costs may fall. In fact, you can demonstrate that with quality controls cost, probably the most effective way to control cost is to manage the quality of the care process. Finally, stable practice patterns actually create an environment in which you can generate valid new scientific knowledge.

For the past 20 years in the United States we have heard a lot about managed care. An argument that I would like to make is despite all this talk about managed care, we have done anything but managed care. In fact, what we have tried to do is manage clinicians, manage physicians and nurses with systems such as utilization review or preauthorization.

What we have discovered as we have conducted these trials is that managed care means managing the processes of care. It really comes down to getting good data in the hands of the people who deliver the care so that they can make informed decisions. We have repeatedly showed that when that occurs, that you get better patient outcomes at a lower cost.

Finally, it should be noted that such efforts require substantial investment. We have demonstrated within our system that those efforts return a very good return on investment. But I think that it should be emphasized that these don't come easily. They don't come cheaply. They take real time and effort to achieve, and one of the things that really concerns me in some of the plans that are being floated, the purported savings don't take into account the amount of effort that is likely to be required to achieve them.

With that, thank you and I think I am ready for questions.

Chairman WYDEN. Doctor, thank you.

[Dr. James' statement may be found in the appendix.]

Chairman WYDEN. We are pleased to be joined by our friend and colleague from California, Mr. Huffington, who has a great interest in medical issues and biotechnology.

I want to recognize him if he would like to make any opening statement before we return to the Members' questions.

OK, the gentleman from Texas.

Mr. COMBEST. Thank you, Mr. Chairman.

Doctors, I am going to—I want to admit something early on in this that this may come as a tremendous shock to you, but I—and I can't speak for my colleagues, but I am not an expert on everything.

When we start talking about medicine, we are talking in an area that is quite foreign to me. Fortunately, many of us have—I am sure all of us have available to us people who are experts and people who are in the industry and people who are close friends or family members, and I have several of both who are in the medical profession.

So my questions to you are going to be basically sort of what my job is, and that is the conduit of them to the Federal Government and to people who are impacting Government.

These are questions and concerns that they have. Obviously if they have them, then I have them. There has not been anyone that I or my staff have visited with that have not indicated their desire for more information.

They are not looking for a lot else to read, as busy as they are, as many things as they have. They don't sit back and think, gee, I wish I had something else to look at. But they are obviously the ones that, in addition to the patients certainly, they are the ones that benefit the most from doing the proper procedures, from using the proper equipment, from making the best decisions that they can make for themselves and the outcome of their patients.

They are concerned about the fact that even within the medical profession, there are varieties of opinions based upon the same information and the final result of that information, and that we are going to discuss further in detail today on some very specifics where there have been reports that say some things, in fact, don't work and some of the people who have talked to me have said, well, in certain cases they do.

Their concern is this: If you have a Federal institute, FDA, whoever, making a determination about which procedure or procedures, if there are more than two, would be the most beneficial, they are concerned that they would take into consideration all of the things that go into that pot to decide which is the best procedure, the age, the degree, how extensive the particular problem may be, that in some instances, 95 percent of the cases may be best treated by one particular device or process that is determined within the industry to be the accepted one, but in 5 percent possibly, one that is not so readily viewed as being available may work best depending upon the condition of the patient.

What they want is the ability to have both of those available so they can pick the tools that are out there that best fit the particular case of their individual patient, and they are concerned that if we begin to—if we set up an agency or a group to begin to establish the criteria for which is the best device for treatment, that that will not be totally inclusive, that will look at, given these conditions, this one may be best, but, however, given these conditions, this one may be best; that it is going to be more generic and it is going to say, well, in 75 percent of the cases this one is the best. That one

then becomes the process which is going to basically be available due to liability, due to insurance, due to Medicare reimbursements.

Those are going to be the ones that are going to come to the surface and other devices that may be better in certain instances may not even be available. That is their primary concern. I think it is very valid, and I would like your comments on that.

Dr. JAMES. I basically agree with your statement. I think the role of the Federal Government is clearly to supply information, not make decisions. We have a body of research that I see by the way where we have carefully asked patients about their perceptions of quality in health care.

It turns out that for about two-thirds of our patients, it depends upon information transfer. You see, that information can't be general. It has to be specific to the illness that a patient faces at a current point in time.

We were a high quality provider if we first explained the disease to the patient, if we told them of the treatment options, if we involved them intimately in the decisionmaking process so that they had some control over what happened in their life.

What I think this sort of program really ought to address is the availability of valid information. Now, I do believe that it is fair to set ground rules as to what constitutes valid information, but I think we are really talking about generating information as opposed to making decisions for American health care consumers.

Dr. WILLIAMSON. I would like to add that in use of that information, as I pointed out in my testimony, expert systems make this much more effective. An expert system with validated information in its knowledge base can then individualize the information we know to a specific patient with that specific patient's characteristics.

The ones that we are using out in Salt Lake even require the physician to discuss with the patient about the patient's values as to what type of outcome the patient may value if there is two widely divergent outcomes that may result from surgery or medical treatment.

Expert systems make this possible and bring in the detail that very few physicians can remember, keep up with, or even keep in their head.

Mr. COMBEST. Thank you very much.

Chairman WYDEN. Gentleman from California.

Mr. HUFFINGTON. No.

Mr. KIM. No comments.

Chairman WYDEN. Any gentlemen from California? All right.

Let me start with you, Dr. James, and I know you are under a tight time schedule. Would you agree with the proposition that as of now, we have two very specific, very significant problems?

The first is that there is an actual shortage of scientific studies and data-evaluating technologies, and second, that there really isn't any practical system of getting information that is known to doctors in a way they can use it. Would you agree with that?

Dr. JAMES. I would agree with both of those statements, especially the first. The second I think we know how to do it; we just haven't implemented, if you see the difference I am trying to draw there.

Chairman WYDEN. There is no question that we know how to do it.

Dr. JAMES. We just haven't done it.

Chairman WYDEN. The problem is the system has never put a focus on trying to get this information out early on, number one, and number two, there has been no practical way to generate the significant funds that are necessary.

Dr. JAMES. That is correct.

Chairman WYDEN. What does it take in your experience to persuade a physician to change their long-established practice pattern?

Dr. JAMES. The single most effective tool we have ever found for dealing with physicians, and I think this goes beyond me, I think this is generally in the field, is good data.

Physicians are trained to respond to data and we have repeatedly found examples where, for example, physicians have cut their salaries in half in the face of data that showed that what they were doing for patients were not as effective as they had believed.

That is the primary factor that drives the physician is the patient outcomes they achieve and data on patient outcomes and the effect of their treatment is clearly the primary motivating factor for determining what care will be delivered.

Chairman WYDEN. Do you think it will be difficult to have a successful cost containment strategy in our country without this kind of information?

Dr. JAMES. I believe that the proposals to contain costs that are not based on data are very likely to fail. They will probably fail in subtle ways. They will take the form of price caps, and I don't believe that those price caps can effectively work without changing the underlying care delivery system, and the most effective way by far to change that underlying care delivery system is, again, better data to physicians on outcomes.

Chairman WYDEN. We are intrigued by the way, Dr. James, you have integrated quality improvement with technological evaluation. Outside of this hearing, those subjects usually come up separately.

Essentially what you have done in your comparative technology study is to make wiser use of an older technology quadrupling your patients' survival rates to the point where it was even better than the brand new high-priced technology.

Could this be done in additional areas other than respiratory distress? If so, we would be interested in any example.

Dr. JAMES. We have done that. We currently have projects under way in 20 or 30 areas, among thousands by the way, within IHC. It clearly applies in a general sense to essentially everything that we do within medicine.

Fundamentally, you can't measure the outcome of a medical technology until you apply it in a consistent way. Quality improvement provides a series of iterative tools for stabilizing a process of care so you can deliver it in a consistent fashion for eliminating variation so you can measure outcomes and systematically improve, and we found it to be a very effective tool where we have created an environment where physicians can lead that sort of a change.

Chairman WYDEN. Your statement, Dr. James, that only 10 to 20 percent of common medical practices have a scientific basis goes a

long way to explaining the pretty puzzling, if not almost bizarre variation, that you see in practice across the country.

Can you provide an example of just how wide a variation there is in physician practices that you have studied to tell us why Congress should be concerned about reducing the extent of this kind of variation?

Dr. JAMES. Well, two quick examples. One I have already given. When we stabilized variation, when we eliminated the variation of how we managed ventilators for adult respiratory distress syndrome patients, it resulted in, we estimate, in a four-fold increase in survival by itself. That is a fairly profound effect.

Beyond that, in 1987 and 1988 in Intermountain Health Care, we tracked six different care processes: Transurethral prostatectomy, total hip arthroplasty, cholecystectomy, coronary artery bypass grafts, coronary pacemaker implantation, and community-acquired pneumonia.

For very carefully balanced groups of patients, for comparable patients, we compared physician-to-physician their treatment decisions and measured the range in variation across groups of physicians.

The smallest range of variation we ever found was about 60 percent. That means if one fellow used 10 of something to get the job done, somebody else used 16 of the same thing to get the same outcome on the same patient.

The widest range we found was about 450 percent. That is a 10 to 45 difference. Interestingly, in sharing those data with our physicians, what we learned are some things. Number one, they didn't know that they were different from one another. They knew there were small differentials. They just had no idea that they had this magnitude of difference.

Number two, they had a profound interest in those differences, as you might expect, and we really asked two questions of our physicians. Number one, why are you different, and number two, given your expertise, you tell us what is the best care for your patients.

Chairman WYDEN. Let me just interrupt. What you are saying then is comparative information is incredibly powerful with a physician.

Dr. JAMES. If it is properly delivered in a safe environment and it compares them to their peers, we found it to be very effective.

Chairman WYDEN. Is it your contention, doctor, that good solid comparative effectiveness studies is generally going to reduce variations?

Dr. JAMES. It has been my experience, but one comment on that. Before I came to IHC, I did randomized controlled trials at Harvard University at the Harvard School of Public Health.

The problem with those trials was that we limited them to very small groups of patients, very carefully controlled groups of patients, so that we could control bias in the study and usually evaluate the efficacy of a new treatment approach to drug or technology.

When you move out into an actual practice setting, it is hard to generalize those very carefully controlled results. What we really need is something you might call a phase four trial or after-market trial where you make comparisons of how care is delivered in a real practice setting, which is the next step that now currently isn't

done, but I think would be a real opportunity, and as I understand it, is exactly what you are proposing.

Chairman WYDEN. It is, in fact, what I am proposing, and let me ask you just one other question on this matter of variation in medical practice, because I share your view that this is an opportunity for significant savings, and again, also a tool for innovation, but some have been critical and have said that reducing the variation in medical practice would simply result in collapsing a practice toward the mean average of practice, therefore reducing your savings and possibly eliminating constructive variation and innovation.

What would be your response to people who have been somewhat critical of the approach, and I gather you have taken on this?

Dr. JAMES. It depends on how you eliminate the variation. A couple of points. First, it needs to be under control of the people who deliver the care. You never aim for the average. You always aim for the best. You always try to find and implement the best as opposed to trying to establish an average performance level.

If you use a quality improvement method, which we use, where physicians are in control of the care, by eliminating the variation, you establish an environment in which it is possible to systematically learn, where you can begin to apply small trials in a regular practice environment to find ways to improve care.

I have had this conversation with a number of my academic colleagues across the country. They particularly raise it in terms of teaching residents. They say that they want to show their residents the smorgasbord of different approaches that can be used.

My reply to them is this: Your real goal in teaching is, number one, to show your residents the current best way to do something based upon the scientific information, and more important still, to teach them how to learn from their own practice in a systematic way. If you have that variation, you can't learn is what it comes down to.

Chairman WYDEN. I know we got to let you run off for a plane, but let me let you go by asking you to comment on the proposal that I am circulating now for input and comment from those in the industry and academia, physicians like yourself.

Dr. JAMES. I am going to translate it in the language that we would use internally. Again, it is the idea of a phase-four trial. We have had two experiences recently that I think illustrate this.

The first was a study of comparative ventilators that we did within our system. We found that some perform better than others. It was an independent study. We had no tie to the manufacturers. Interestingly, as we prepared to publish that, some of the manufacturers who had not been rated well threatened legal action if we published our results, fairly clarion attempt to delay release of those results because they saw an economic disadvantage if those data become widely spread.

On the other hand, more recently we were contacted by a company who has invented a new technology to remove surface antigens from red blood cells. That means you can take type A blood or type B blood and make it into type O blood. It can have some very significant cost implications for how you manage a blood bank and just the availability of a clean blood supply.

Interestingly, they contacted us very early in their development process. They understand that to effectively use this new tool, they don't just have to show that it works, that it will remove antigens from the surface of red blood cells and to show that it is safe to give to human beings, they want to show how it fits in a real health care delivery system. They want to understand how to apply it and what implications it has.

Now, we sometimes call those phase-four or after-market trials, that ability to understand how a technology applies.

I think that your proposal addresses that critical issue, and I think it could be a real contribution to our ability to understand best care delivery practices.

Chairman WYDEN. I appreciate that, and I want you to understand that we are very interested in this after-marketing, post-marketing phase as well.

There are kind of two efforts to this, the premarketing, but we also want to address the later stages.

Dr. JAMES. You see, in my translation that is what your proposal really addresses is our ability to understand those sorts of issues, and it clearly supports our ability to generate those kinds of data.

Chairman WYDEN. We will excuse you. I understand you have got a 11 o'clock flight at National.

Larry Combest can usually make it in 15 minutes, but we will allow you a little more, and we thank you for all the help you have given.

Dr. JAMES. Thank you, very much.

Chairman WYDEN. Dr. Williamson, let me ask you a few questions as well. The subcommittee has heard about a long discredited treatment involving, quote, "intermittent positive pressure breathing equipment."

In one recent journal article it said it took over 10 years to get to the point where only 20 percent of American hospitals routinely use this practice. Why isn't that the pace of technology diffusion when a new expensive technology is brought to the market?

Dr. WILLIAMSON. Well, when a new expensive device or technology is brought to the market, you have to be very careful about the fact that you will not have any long-term data upon which you can identify unintended negative effects, and you have to then weigh the lack of that kind of information versus the efficacy and value you have already received from the previous technology.

But, again, most of these decisions are not straightforward. They have pluses and minuses and in any given situation you would have to be very careful as to whether the advantages of a new technology will outweigh the disadvantages that might accrue.

Chairman WYDEN. Under virtually all of the health reform proposals it is anticipated that there would be a lot of pressure on payers and practitioners to cut costs.

What do you think about the chances of success by payers attempting to achieve efficiency and economies if physicians aren't persuaded of the need to change practices based on data?

Dr. WILLIAMSON. I think one of the points that will be emphasized under health care reform is the measurement of outcomes, and if we have—and we do have valid instruments, for example, for measuring quality of life, and if we can measure outcomes and we

see that they are starting to deteriorate under whatever cost savings policy are being used, then, of course, we have got to do something.

But another method, and one of the problems under reform is that tendency to under utilize. There will be—you can save money in managed health care if you make your staff work harder and—for less, do more for less, and you can burn them out.

But if we are going to do random samples of consumers to identify their satisfaction, I would suggest we have got to do random samples of providers to identify their satisfaction, and you have to balance these two to see whether or not these policies for cost cutting and cost savings are having, again, unintended negative effects on your own staff while you are saving money for the consumer.

Chairman WYDEN. Your accounts about the value of what you call expert systems to aid patients and physicians in putting medical knowledge to work are impressive, and I think very worthy of further review.

How ready for public use is this kind of technology?

Dr. WILLIAMSON. Well, this technology is just now developing, and I would say that it is going to be several years until we will have proven, ready to use expert systems, but they are very promising and many people who I know that have been studying the various technologies of disseminating the results of research indicate that it looks like expert systems do look like the most promising, but they are still in an early stage of development, and we are several years off before they are going to be really sound and that we can get them out and widely applied.

Chairman WYDEN. You would, I gather, anticipate at first it would be used by physicians—excuse me, by patients in a physician's office, and at some point presumably people could get it at home through their television and a cable hookup?

Dr. WILLIAMSON. Exactly, exactly. In fact, we are now doing the initial pilot testing of an expert system we call home Iliad that facilitates consumer decisions. It helps them identify when they should get into see their doctor, what things they can take care of themselves, what are the danger signals.

It gives them that kind of information, as well as something that is more important that I emphasized, helping them take their own history by use of this type of system.

We know today that history taking is probably the single most important reason for diagnostic error, and diagnostic errors are increasing rapidly under current practice.

Chairman WYDEN. We will be very interested in pursuing this with you as well, doctor. I very much appreciate your interest in the proposal. I think your suggestions are on point as well, and frankly, as you listen to this discussion, you constantly see first how health care is behind.

What I think is so staggering as you look at the physicist community, electronic bulletin boards, a way to get information out, in the environmental area this is now happening, we are really playing catch-up ball in terms of trying to get comparative data out in terms of medical technology, and at the same time as you go a little

ways down the road, you could see how people could abuse it and it could be misinterpreted.

The first thing that I think about, I think your suggestion in terms of an expert system makes a lot of sense, you have to say to yourself, particularly as you look toward home use, that somebody is going to try to come up with a knock-off, some kind of quack system, and all of a sudden people are going to be misled and the like, and I think we can get support in the Congress, bipartisan support, for a system that incentivizes the private sector to come forward with this data and also look at some of the technological wonders you are talking about for getting it out, and we are going to consult with you very closely as we pursue this.

Dr. WILLIAMSON. Thank you.

Chairman WYDEN. Happy to recognize the gentleman.

Mr. COMBEST. One more question came to my mind. This is one of those you can't get wrong on a test because it is one of those, in your opinion, questions.

In your opinion, do you think that the liability question has any impact upon the decision of a physician not to move to a new procedure, to stick with one which has been tried and true and that they have confidence in?

Dr. WILLIAMSON. It is unfortunate that we have very little, if any, valid data on the subject of defensive medicine, but in my opinion, I would estimate that—and others have estimated from 10 to 30 percent of the interventions that are ordered are not for the benefit of the patient, but to protect the physician against liability, and I think that the studies that were done at Harvard in terms of cat scan indicated that up to 85 percent of the times they were ordered, it was not for the benefit of the patient, but more to protect the providers from the court battles and the liability, as you say, that they would face.

So I think it is a substantial problem and this is where we need tort reform to help remove this risk.

Mr. COMBEST. Thank you, doctor.

Chairman WYDEN. Before we go, let me pick up on my colleague's point because I think it is an important one.

First, it seems to me that doctors have got to be better off if the scientific basis of their practice is understood and known; is that correct, Dr. Williamson?

Dr. WILLIAMSON. Yes.

Chairman WYDEN. I coincidentally happen to support tort reform, malpractice reform as part of the national health reform bill. I do it more because I think we are going to have to ask all the stakeholders to accept some changes.

We are going to ask insurers and providers and drug companies and everybody else to do it, you got to recognize that the legal system is going to have to be changed as well, but I think this point of trying to provide an understood coherent scientific basis for a doctor's practice has got to do more to provide relief than almost anything else.

Even having that said, I am prepared to support malpractice reform. Mr. Combest and I have the pleasure of voting on all this.

Dr. WILLIAMSON. I guess you can see by my own career that in trying to facilitate improving quality of care, I went to science in-

formation management as the key to doing this, and this is exactly what this bill is trying to do, and I really applaud your effort.

Chairman WYDEN. I thank you for your comments, for your interest, and we are going to be working very closely with you.

Dr. WILLIAMSON. Thank you

Chairman WYDEN. Our next panel will provide us examples of clinical evaluations of technologies. The subcommittee has assembled on this panel an array of medical technology assessment talent to discuss certain widely used medical technologies.

Their findings with respect to established technologies, in the view of our staff, have much to teach us about this need to perform similar evaluations on medical technologies while they are still new technologies before live money is wasted.

We are especially interested in their advice as to how the quality of these comparative technology evaluations can be assured, and let me bring forward at this time Dr. Topol, chief, Cardiology at the Cleveland Clinic, Dr. John Burke, clinical epidemiologist, LDS Hospital in Salt Lake City, Dr. Jerry Avorn, director, Program for the Analysis of Clinical Strategies at the Gerontology Division at Harvard.

Cheers for all and we welcome each of you. Thank you for your cooperation with us. It has been the practice of our subcommittee to swear all the witnesses. Do any of you have any objection to being sworn as a witness? Please rise and raise your right hands.

[The witnesses were sworn.]

Chairman WYDEN. We are going to make your prepared remarks a part of our hearing record. If you could each take about 5 minutes or so to summarize your principal concerns, it would be helpful, and we will make your prepared remarks a part of the formal record.

Dr. Topol, welcome.

TESTIMONY OF ERIC TOPOL, M.D., CHAIRMAN, DEPARTMENT OF CARDIOLOGY, THE CLEVELAND CLINIC FOUNDATION, CLEVELAND, OHIO

Dr. TOPOL. Thank you. I would like to first emphasize that the randomized clinical trial format is really a pivotal one, and while we talk about data, that in fact the best data we can provide, the best yardstick for comparing alternate technologies really resides in the comparative randomized prospective control trial, and there really is a substantial dearth of these trials today, and so the points made by our previous panelists in the discussion that a relatively small proportion of our information that we know and we use for medical practice is coming from these clinical trials.

So even with the best intentions, clinicians applying therapies to patients are often faced—have the absence of controlled proof of efficacy. In order to do these trials, it is very important to point out that they are quite time consuming, they are expensive, or can be expensive, and they really require physicians and manufacturers to state up front that we don't know, that we don't really have a proof—or a validation of the use of a newer technology compared to the established standard.

So our current system really has many disincentives to perform randomized clinical trials. In working with the Agency for Health

Care Policy and Research in development of guidelines for clinical practice, it has been quite evident to me that this process resides very much on expert opinions and there is very limited hard data, hard documentation for choosing a particular recommendation in these official AHCPR guidelines.

So it is interesting to note that many of these experts' opinions can prove to be wrong at a later date.

So really it would be best if we could to amalgamate the resources and provide the incentives to promote more randomized clinical trials and provide that hard data, the definitive data to make important decisions.

I would like to go through very briefly the randomized trial that we did, which was mentioned. This was a large randomized multicenter trial, multinational trial at 33 sites in the United States and three sites in Europe comparing a new technology in cardiology known as coronary atherectomy in which the plaque of the coronary artery is actually shaved out as compared to the established technique over the past 16 years known as balloon angioplasty where the artery is just simply stretched.

This technique of atherectomy where the plaque is actually removed was introduced investigationally by the FDA in 1986, late 1986 and it was approved for commercial use in September 1990. In the first year of its availability in 1991, there were 17,000 procedures performed in the United States This was at an equipment cost of approximately $35 million.

The rapid acceptance of the technique was very much tied into the anticipation that there would be improved outcomes of less recurrence, less complications by having the ability to take the plaque out rather than to stretch the channel of the artery.

In 1992, there were more than 33,000 procedures performed, and this year there will be more than 60,000 procedures performed in this country. The results of our trial of over 1,000 patients, and interestingly it is the largest medical device trial yet to have been performed, randomized device trial, this was very helpful and insightful because what it showed was very counter to what was expected, that, in fact, the complication rate, and particularly the heart attack rate, was increased in the atherectomy group.

The need for repeat procedures was not reduced at all during the extended follow-up period, and the cost was increased, $1,300 of actual costs more per patient for use of the atherectomy compared with angioplasty.

So this trial was very helpful, and still although atherectomy is an important advance, and that should be emphasized, and quite useful for select patients, the data certainly indicates to us that until the procedure is improved, it is not suitable for wide application.

This is a nice example, we believe, that a trial can be done quickly, that it can be done soon after the PMA approval from the FDA and within a short period of time with a large number of patients, we can get some valuable data which proves to be meaningful for clinical practice, and as it turns out, to reduce costs.

So to sum up a couple of points, it is clear that we can do trials in a timely fashion, but, unfortunately, they can be expensive. This particular trial that I have used as an example among many that

we have done over the past decade costs actually just over $2 million to perform.

Now, this can be quite sizable to a small company and it would be ideal if we could find some other ancillary ways to provide support, because the information derived from these trials is important, not just to the company, to the patients, to the providers, but also very much to the payers and to the Government.

So there really should be an alliance to create a favorable environment that provides incentives beyond the exclusivity which is quite reasonable and beyond the other parts of the proposal that you have outlined to share the burden as far as the research costs, which are important.

So I think that currently there is a blind spot in our system. The FDA does not review, having worked and continuing to work on the advisory panel of the FDA, we do not factor in cost in any decision. It is simply safety and efficacy. There is no dimension of cost in the assessment.

The AHCPR works on providing guidelines in some selective research, but that is also not comprehensive and as we talked about, very much relies on expert opinion guidelines which are quite subjective. So we really do need a better system to encourage meaningful research of new technology in the future.

Thank you.

Chairman WYDEN. Doctor, thank you. It was very helpful and we will have some questions in a moment.

[Dr. Topol's statement may be found in the appendix.]

TESTIMONY OF JOHN BURKE, M.D., CHIEF, INFECTIOUS DISEASES, LDS HOSPITAL, SALT LAKE CITY, UTAH

Chairman WYDEN. Dr. Burke, welcome.

Dr. BURKE. Thank you, Mr. Chairman.

My name is John Burke and I am a physician. I am the chief of Infectious Disease at LDS Hospital in Salt Lake City, Utah.

For the past two decades, I have led a research team that has studied the effectiveness of drugs and medical devices. I am concerned about the survival of the species of people like myself and how your legislation could help ensure our survival.

My experiences as an investigator have led me to the conclusion that our system for evaluating medical technology is badly flawed. Ideally, a synergy of Government, industry, and independent clinical researchers would support the evaluation of drugs and devices.

Unfortunately, at the moment, not only does industry often seem wary of large scale clinical trials, but Government agencies tend to unnecessarily delay clinical research. In the absence of medical facts, patients suffer needlessly and the Nation's hospital bill grows unnecessarily.

Today I want to encourage legislation to streamline the process for clinical evaluation of drugs and medical devices.

I have personally encountered many of the problems that now plague our system, and I offer three valuable lessons. First, that the fundamental component for evaluating medical technology is the large scale clinical study. Second, that subjects in these studies must be typical patients, not carefully selected patients only for randomized trials, and third, that medical device law as currently

existing does not adequately assess even safety, let alone efficacy of devices.

With so much at stake, manufacturers dare not expose a new product to large scale clinical testing for fear of discouraging results. Instead, manufacturers contract for small studies, in carefully chosen populations, that promise favorable conclusions.

Such research may be less than independent and impartial since the manufacturer has the motivation, if not the ability, to suppress contradictory results.

Furthermore, manufacturers often begin promoting a product even before it is tested and before that testing is complete. Thus, advertising claims may amount to nothing more than wishful thinking. The net result is that new drugs and devices arrive for patient use before their efficacy and cost-effectiveness have been established, and it is an unhealthy and a dangerous situation.

As an example, my colleagues and I recently conducted one of the many studies that illustrate these problems. We studied a silver coated urinary catheter that you mentioned earlier. Ordinary catheters are made of latex rubber and are prone to causing infection and manufacturers had hoped that by coating the surface of the catheter with a disinfectant, such as silver, that the risk of infection might be reduced.

This innovation addressed a serious medical problem. Urinary catheterization is the most common cause and most common source of fatal bloodstream infection, and the costs from the side effects of the urinary catheter may add as much as $2 billion to our health care bill every year.

Now, the silver catheter arrived in the hands of doctors after a single clinical trial. That trial was small and poorly designed. It tracked a mere 74 patients who were not representative in any way of the general hospital population, and worse, the design failed to control for the variable being tested.

Additional disinfectants had been added to the system making it impossible to credit the silver coating with reducing the rate of infection.

Yet, it was this flawed study that was used to convince hospitals, doctors, and patients that the silver-coated catheter was worth its higher price tag, three to four times that of the ordinary catheter.

Unfortunately, the advertising pitch was more effective than the product. Soon after its introduction, when we began our study, the silver-coated catheter had captured 20 percent of the market in our area. We then tracked 2,500 patients in a large scale clinical randomized trial.

Our patient sample was not only statistically valid but representative of the patient population, and our results contradicted the small premarketing study.

We found that the silver catheter offered no benefit to patients, and even worse, male patients actually suffered a significantly higher rate of infection. Thus, rather than lowering the rate of infection and cutting overall costs, the silver-coated catheter hurt patients and increased their bills.

Clearly this device was dangerous to their health and to our health care system, and it was unsafe at any price.

We conducted our research with these catheters with our hospital's sophisticated computer data base for medical records. We have used this system to not only monitor, but more importantly, to improve clinical practice. For example, we sought to prevent adverse drug reactions in patients, a problem that afflicts 3 percent of our hospital's patients, adding about $1.7 million annually to our hospital costs in our own individual hospital.

We began this project by collecting data on the incidence of adverse reactions and we quickly realized the shortcomings of information about drugs that are collected during prelicensure testing. Most drug trials for licensure understandably include patients receiving only the experimental therapy, but such testing is only the first step.

Drugs must also be tested under real clinical conditions, the so-called phase four study when they are often used in combination with other drugs.

Our findings confirmed the need for such studies. We discovered, for instance, in the case of one antibiotic known to cause convulsions in some patients that the seizure rate was, in actual use, more than twice the rate predicted by its manufacturer.

Our research suggests that this was not an isolated case and that the surveillance of drugs must continue after they reach the market and the public.

We have also used our computer system to determine the efficacy and cost-effectiveness of drugs used in the hospital, a topic that has largely eluded scrutiny. At the LDS Hospital, by reviewing the cost outcomes of various antibiotics and then altering clinical practice, we achieved dramatics savings, despite the increased use of newer, more expensive antibiotics.

In 4 years, in fact, the percentage of our pharmacy budget spent on antibiotics dropped from 42 percent to 14 percent, and more importantly, we provided our patients with better care.

Our studies highlight the importance of large scale clinical trials of both medical devices and drugs. The potential for cost savings and improved patient care is tremendous. As we have shown, health care costs can be cut by improving care.

This should be a major focus of health care reform. Yet, there now exists a funding gap for studies like ours. Neither the NIH nor the AHCPR accepts responsibility for funding these types of studies. In the past, our studies were supported by the NIH. But now neither of those agencies is targeting and supporting promising and necessary clinical research, nor has industry stepped in to fill the gap.

We must take steps to achieve synergy with industry, Government agencies, and independent researchers.

Whatever the specific directions of reform, I believe that incentives for clinical research must be emphasized and that legislation should provide drug and device companies with inducements to fund large scale clinical trials. For example, by lengthening the period of patent protection and streamlining the approval process, more and better drugs and devices might arrive on the market expeditiously.

Preliminary FDA approval that would restrict use to certain sites where intensive surveillance would be conducted is an option that

should be explored, and a fast track for FDA approval of drugs and devices would encourage both innovation and evaluation, bringing industry, independent researchers, and Government together in the process.

Thank you.

[Dr. Burke's statement may be found in the appendix.]

Chairman WYDEN. Thank you, Dr. Burke, and I appreciate you speeding up when the egg timer went off and we feel badly about being short. It is going to be a hectic morning and we will have some questions for you and Dr. Topol.

TESTIMONY OF JERRY AVORN, M.D., DIRECTOR, PROGRAM FOR THE ANALYSIS OF CLINICAL STRATEGIES, GERONTOLOGY DIVISION, HARVARD MEDICAL SCHOOL, BOSTON, MASSACHUSETTS

Chairman WYDEN. It has been excellent and I know Dr. Avorn will be as well. Doctor, let me thank you as well for the many hours you have spent in our office consulting with both Mr. Schulke and myself and please proceed.

Dr. AVORN. Thank you, Mr. Chairman, members of the committee. Thank you for inviting me here today. My name is Jerry Avorn. I am an internist, geriatrician, and a health care researcher at Harvard Medical School and the Brigham and Women's Hospital in Boston, which I guess today I should refer to as the Salt Lake City of the East.

I am pleased to share with you some ideas on how we can make the Nation's great resources of medications and medical devices better serve the needs of our patients at a time of increased cost containment and calls for expanded access to health care.

My comments today are based on the work of our research group at Harvard as well as input from an expert panel on medications and aging, which I had the privilege of assembling with a grant from the Hartford Foundation.

Much of what I will have to say refers to both the elderly and the young, but as in many instances in health care, these issues are in boldest relief in relation to the other.

I want to start by deflating a myth that is believed by many, perhaps by most Americans. The myth is that when you go to visit your physician, he or she is armed with adequate information about the advantages and disadvantages of the common medications used to treat your particular problem, compared to one another. It is a plausible myth.

I too would like to believe that as I get ready to write a prescription or when I teach medical students or interns and residents, I could turn to a solid base of research data to help answer the following real world questions: Which of the many available arthritis drugs is the most effective for the commonest form of this disease, and which has the lowest risk of potentially fatal side effects?

For a man with difficulty urinating and an enlarged prostate gland facing the options of prostate surgery or long-term use of medication or simply watchful waiting, which alternative is most likely to provide the best relief of his symptoms with the fewest complications?

Some drugs are available to treat high blood pressure at a cost to the patient of under $10 for a year of therapy, while other high blood pressure pills can cost over $1,000 for the same year of therapy. How do these drugs compare in their side effects and in their ability to prevent the long-term complications of high blood pressure, such as stroke, which is after all the main reason we treat hypertension.

How do all these questions differ in their answers if the patient is 80 years old rather than 50?

The information that I need as a doctor to adequately answer questions like this is simply not there, and it is not there for any doctor in the country. This is because it is presently no one's responsibility to do the research needed to generate such information or to make sure it is available to the practicing physician when he or she makes recommendations to the patient.

Let me be clear why this is the case. The Food and Drug Administration has the mandate to make certain that all drugs approved for use in the United States are safe and effective, and by and large, it performs this task well, but it is not the legislated mission of the FDA to compare drugs with one another to see which is better or which is more cost-effective.

In fact, the main requirement imposed by FDA is for a drug manufacturer to show that its drug is better than nothing or a placebo. FDA officials will be the first to point out that it is not their job to evaluate drugs beyond this point and they seem to have no enthusiasm for taking on this role.

Nor is it prudent public policy to expect the drug manufacturers will come forward voluntarily to subject their products to tougher testing than is required of them. Companies do engage in some comparative evaluation if it is likely to show their product in a good light, but that leaves a lot of important comparisons untested.

Foremost among these are comparisons with time tested old standby generic drugs, which very often are every bit as good as and in some cases even better than much more costly patented drugs. However, there is very little reason for companies to fund studies to evaluate these inexpensive drugs on which no one is making huge profits anymore.

So there really are two components to this myth about how much information is available to your doctor when he or she is writing a prescription. First is the myth of the kind of comparative information that is in existence, which it is not, and second is the myth that it is the responsibility of some organization or industry or set of individuals to make sure that such data are in place. No one has such a responsibility.

This is not because such information would be impossible to generate. It would require large-scale clinical trials, as Dr. Topol has mentioned, observational studies of huge numbers of treated patients, and epidemiologic studies of populations. These can all be done.

My colleagues and I at our research unit do this kind of work, as do others at the table, and it is frankly much less difficult than many other kinds of research. The problem is there is not much interest, as was just mentioned by Dr. Burke, in supporting such research.

FDA has very little money available for university-based investigators and does not see its mandate as including this kind of work. The National Institutes of Health sees its role as supporting basic biological research and often has a rather condescending attitude toward mundane studies comparing different ways of treating patients' problems.

People have suggested that the pharmaceutical industry might be a plausible source of support for this kind of drug research, since at present their research budget within the industry is greater than the research budget of the entire National Institutes of Health.

NIH, therefore, assumes that such studies ought to be supported by industry. However, it is naive to think that a company that has invested a nine figure amount in developing a drug will be enthusiastic to support it—I am sorry, to subject it to a costly study comparing it head-to-head with an older product that may cost a 10th or a 50th of its price and might work just as well.

There is a small agency that has been mentioned, the Agency for Health Care Policy and Research. It has an enormous mandate and a tiny budget which has not been adequate to meet the needs of all the research that is needed in this area. There are people out there who could perform this research admirably.

Our university and teaching centers are full of people with adequate training and enthusiasm who have seen in their own practice and in their own medical education the disparity between what is known and what is needed to be known.

Yet, as was mentioned by Dr. Burke, this is an endangered species that finds it very difficult to persuade others that it needs the funds and should get the funds to do its work.

Given the current budget deficit, this is not a good year to ask for another way for the Federal Government to spend money. This is a paradox since it is also a year in which we are discussing having the Federal Government underwrite several billion dollars of medication costs for the elderly.

But even now, the Federal and State treasuries are spending tens of billions of dollars per year to pay for drug coverage through Medicaid. If a fraction of that money were spent on this kind of comparison of alternative therapies, the investment would be repaid almost immediately.

There is one source of support that has not yet been devastated by the budget deficit, and that is the private sector. If we could galvanize employers, insurance companies and HMO's who will be picking up large chunks of this $70 or $80 billion a year we will be spending on drugs in the next few years, if we could galvanize some of that interest and some of that commitment to devote it to the capacity to do this research, we would be able, I think, to have a very wise investment.

What is needed here is a catalyst and this committee may well be suited to provide that kind of leadership. Payers in both the private and public sectors need this information; practicing patients want it, and the patients of this country deserve it.

We are not needing to spend more money on health care. We simply need to spend it more intelligently.

We do not want to move to a situation in which cost containment means you pick the cheapest way to go, because the cheapest way may not be the best way. It may not even be the most inexpensive way if it turns out that a more expensive therapy can generate far better outcomes down the road, prevent hospitalization, prevent disability.

It may be that what looks like an expensive product may indeed be the most cost-effective one. We need elegant kinds of analyses of the sort that Dr. Hillman and colleagues do in order to find out what truly is cost-effective.

In closing, let me just make one final observation about how this relates to the movement toward health care reform. One key missing link that seems to be absent in virtually all of the plans that have been put forward for affordable health care is the idea that there is somehow knowledge out there that physicians can be made to apply if only the economic incentives are available.

The knowledge is not there. It is not possible for even the most well-motivated intelligent physician to make all the right decisions in the absence of inadequate data base, and I think a very constructive outcome of the sort of program that you have described would be making that information available so that with the economic incentives in place, physicians could indeed make more intelligent, cost-effective choices for their patients.

Thank you very much.

Chairman WYDEN. Doctor, thank you, and your testimony along with your colleagues has been excellent and we will have some questions in just a moment.

[Dr. Avorn's statement may be found in the appendix.]

TESTIMONY OF ALAN HILLMAN, M.D., M.B.A., DIRECTOR, CENTER FOR HEALTH POLICY, UNIVERSITY OF PENNSYLVANIA

Chairman WYDEN. Dr. Hillman, welcome.

Dr. HILLMAN. Thank you very much for the opportunity to be here. Another name for the subject of my testimony today is "the place of effectiveness research in health care reform."

Effectiveness research is a field of investigation into the ways physicians actually practice and you have been hearing a lot about that by my colleagues here. It is also a field of investigation into the ways patients actually behave and respond and the ways to identify the true costs and benefits of medical interventions.

New interventions that work well in theory or clinical trials do not always work as well in actual clinical practice because of poor patient compliance, high cost, untoward side effects, or other reasons.

Currently available medical information does not focus on the sufficiently broad spectrum of outcomes, thus limiting the decision-making abilities of physicians, patients, and payers. The mandate of the FDA, as you have heard, has been to determine safety and efficacy rather than cost-effectiveness and outcomes.

This is necessary, but it is not a sufficient criteria for making clinical and allocation decisions.

Although outcome research in the form of cost-effectiveness analysis has been mandated by regulation in other countries, for exam-

ple, Australia, it is the marketplace in the United States that is demanding better information on true outcomes.

As we continue to move toward a more competitive health care environment, purchasers of health care services are starting to demand information about the true total cost and the true outcomes of new interventions. In and of itself, I believe this demand would eventually encourage most drug device manufacturers to undertake good outcomes research.

However, there is a problem with this approach. Manufacturers of drugs and devices currently are prohibited by law from using most effectiveness information to market their products. They are restricted to marketing only on the basis of their FDA approved labeling which often does not reflect how doctors usually practice.

In addition, manufacturers currently are unclear, as you have heard from my colleagues, about FDA constraints on the use of effectiveness materials. No one is certain about what is permitted and what is not, and this is not a criticism of the FDA because regulating outcomes is not part of their mandate.

However, this problem constrains the medical drug and device industry from responding to marketplace demands for more effectiveness information. I think this is a key and critical issue.

Incentives to facilitate outcome studies by the drug and devices industry will help to encourage the quantity and quality of outcomes research that the marketplace needs and wants. However, the FDA or other regulatory agencies that grant such incentives must be clear about the ground rules.

At a minimum there should be regulatory release of the drug and device manufacturers who produce high quality, valid, and reliable effectiveness information, may use it in their marketing materials and in their negotiations with managed care, managed care formularies, hospitals, and other purchasers.

Regulatory relief in the form of a consistent, simple policy toward the use of effectiveness and outcome information like we are talking about in marketing would be extremely helpful in encouraging more of this type of research.

With respect to your specific proposal, I think it is essential that the key terms be defined accurately. What is meant by, "clinical studies and clinical superiority?" What is the threshold for a drug to be considered, "significantly lower in price?"

Most importantly, any agency charged with awarding special incentives must be capable of evaluating effectiveness research and clear about what the rules are.

All effectiveness analyses must be peer reviewed prior to publication, just like in any true scientific endeavor.

At my institution, 13 pharmaceutical and biotechnology firms are sponsoring a joint public-private academic task force that I direct through no-strings-attached grants to the University of Pennsylvania.

This group is discussing and writing voluntary principles for the conduct and publication of effectiveness related research related specifically to pharmaceutical and biotechnology products. The task force is composed of individuals representing different stakeholder constituencies, including the Government, trade organizations, aca-

demic medicine, medical ethics, private sector research, managed care, medical journals, and the pharmaceutical industry.

High quality effectiveness information will facilitate the allocation of resources by payers, providers, and society. Creating an environment that nurtures this information is essential, and I support the spirit of your proposal.

Thank you very much for your attention and consideration and I was delighted to finish before the bell went off.

Chairman WYDEN. You have been very helpful.

[Dr. Hillman's statement may be found in the appendix.]

Chairman WYDEN. I want to make sure I understand one thing. You all, with some biotechnology companies, are looking at voluntary principles to, in effect, do some of the comparative analysis with a special focus on cost-effectiveness?

Dr. HILLMAN. Exactly.

Chairman WYDEN. We would be very interested in seeing that because that is exactly what I think we want to try to excavate from the industry and academia is the best sense of how to go about doing that.

So we will hold the record open for any information you can give us on that and want to keep special tabs on that as we refine this idea.

Chairman WYDEN. Dr. Marshall, welcome, and we really appreciate your coming. I know it was short notice for you as well and we are very grateful for your involvement

TESTIMONY OF BARRY MARSHALL, M.D., ASSOCIATE PROFESSOR OF MEDICINE, UNIVERSITY OF VIRGINIA

Dr. MARSHALL. Thank you, Mr. Chairman. It is a great honor to testify before the committee and rather unusual, I suppose, to have an Australian before a congressional committee.

My name is Barry Marshall. I am a medical practitioner trained in Perth, Western Australia, but also qualified as an internist in the United States. I am a permanent resident of the United States and have lived in Charlottesville, Virginia, since 1986. I am an associate professor at the University of Virginia in Charlottesville.

Peptic ulcers, my specialty, affect about 1 in 10 persons or 4 million people currently either have gastric stomach or duodenal ulcers in the United States. Typically, peptic ulcers or ulcers exposed to acid are shallow holes in the lining of the stomach or adjacent intestine.

They come and go during life, sometimes causing severe or even fatal internal bleeding.

Until recently, the only cure for peptic ulcer was stomach surgery. Most ulcer patients experience recurrence of their ulcer within a few months of stopping medication. Many ulcer patients must therefore take medication continuously costing about $50 per month.

The medications commonly used are called H2 blockers and have brand names such as Tagament, Axid, Zantac, and Pepcid. Sales of these drugs total approximately $2 billion per year in the United States, half of this being used by ulcer patients.

In addition, ulcer patients often require expensive investigations, such as upper GI series for about $400 or endoscopy which can be between $400 and $800.

In 1982, I discovered that nearly all persons with peptic ulcers were infected with a new type of bacteria, which we now call Helicobacter pylori or H-pylori for short. The new bacteria infected the lining of the stomach and caused inflammation called gastritis. We knew that gastritis was present in most patients with ulcers so it was a simple stick to conclude that if we eradicated the gastritis, the ulcers might heal.

If the bacterial infection could be cured, then the gastritis would heal and the ulcers would be permanently cured.

In 1984, I discovered that H-pylori could be cured with a 14-day treatment consisting of bismuth, which is one of the components of Pepto-Bismol with an antibiotic, and the cost of that treatment was about $40 once.

Since then, an improved version with two antibiotics and Pepto-Bismol has been shown to give an 85 percent cure rate of ulcers, and in Virginia at Peoples Drug this treatment costs $42.

I presented this at a—this double-blind study at the American Gastro Association in May 1987, which is 6 years ago. The paper was published in the Lancet. In other countries, including the United States, researchers were able to duplicate this work, all showing cure of ulcers after eradication of Helicobacter pylori, and several papers have now described cure of duodenal ulcer after this type of treatment.

The old strategy therefore is to ignore the presence of this bacterium and treat the patient with H2 blocker drugs at a cost of about $600 a year. After an initial 4 to 6 weeks of treatment to heal the ulcer, the patient may cease the drugs and wait for the ulcer to recur and perhaps be admitted to the hospital, or may continue to take the drug in half dosage to protect him from the ulcer.

The new strategy is to test the patient for H-pylori when he develops ulcer symptoms through a blood test or a breath test. If H-pylori is present, then antibiotics may be prescribed, as well as the short course of ulcer treatment.

In this way, most patients only need to be treated once in their lifetime. They probably do not transmit H-pylori to their children and the so-called hereditary disease of peptic ulcer is permanently cured.

Currently some doctors recommend that only patients with ulcers receive treatment for H-pylori. In other words, after finding H-pylori, say with a blood test, doctors must then detect an ulcer as well before treatment starts.

This means that the expensive investigations above would still have to be done.

Alternatively, if H-pylori is present and symptoms are compatible with an ulcer, doctors might just treat the H-pylori in any case, thus if an ulcer was present, it would be cured and if an ulcer was not present, then the H-pylori would be cured and the patient would be protected from developing an ulcer in the future with a 1 percent risk per annum.

With the old treatment, the ulcer is not cured and tends to recur. With the new treatment, the ulcer is cured, and suddenly the ulcer

is just like a strep throat, a bladder infection, or sinusitis. Ulcer disease does not need to be feared. No lifestyle modifications are necessary, and patients need not puzzle over the often overrated component of stress.

On page 5, you see a table which shows the estimated cost and cost saving per year for patients treated the old way in the top row versus the new way for antibiotics. It is estimated that if this new treatment is used in the United States to treat all patients with peptic ulcers who have Helicobacter pylori infection, we would save $3,000 per patient over 5 years, and for 4 million people who comes to a total cost of $12 billion with the old treatment, or approximately $1 billion for the new treatment, or savings of $1 to $2 billion per year, and you can play around with these figures any way you like, but we come up with that $1 to $2 billion savings.

Now, unfortunately, these savings were estimable in 1987, 1988, but because these new treatments were so cheap and competed with a very profitable expensive treatment and went against the old dogma, they were not properly evaluated in the United States and, in effect, the company that originally sponsored my research in the United States, Procter and Gamble who make Pepto-Bismol, are currently not doing very much research into this new treatment because they think that it will be too expensive and it is too risky to evaluate a complicated but simple, cheap treatment such as this in the United States and get it through the FDA.

In summary, I would say that new drugs—the United States has the highest standard in the world for the approval of new drugs. Perhaps because of the litigation here, mistakes in earlier approval are far more likely to have severe consequences for drug companies than the Government or the Government bureaucracy who makes then.

New drugs are tested in very selected groups of patients and sometimes these selected groups do not reflect real life, and new study designs should encompass large groups of patients in real life situations.

To make this affordable, the FDA may have to be cost conscious and assess the risk benefit of its very tight standards.

For example, after initial evaluation, some studies could be done in a primary care setting with remote monitoring by mail, telephone calls, or less frequent doctor visits, and this type of approach may be appropriate when drugs have already been evaluated and used in other countries.

Thank you.

Chairman WYDEN. Doctor, thank you.

[Dr. Marshall's statement may be found in the appendix.]

Chairman WYDEN. All of you have been excellent panelists. It is time to talk about the need for comparative medical technology information in the abstract, but what you all have done is drive home how important it is in the real world and the consequences both in terms of patient's lives, in terms of waste in resources what this debate is all about.

So you all have been very helpful. I am going to have some questions in a moment.

First, I want to recognize my friend from Texas—the gentleman from Massachusetts. If we might, the gentleman from Massachu-

setts is from an area where there is great interest in biotechnology. He has been a very welcomed member of the subcommittee. Gentleman from Massachusetts like to make any opening statement?

Mr. TORKILDSEN. No opening statement, but whenever we get to questions, I would appreciate that chance.

Chairman WYDEN. Very good. Let's proceed with Mr. Combest, recognize you next.

Mr. COMBEST. Thanks, Mr. Chairman. Some of—a lot of maybe what we say many times sounds as if we are repeating ourselves, but we are using this to establish some kind of a track record for the future, and if it is not used as congressional intent, maybe at least it is used as something we can look back and say, see, I told you so.

I was interested, Dr. Hillman, in some of the things you had said, and I totally concur that there needs to be some very definitive guidelines that are imposed about—and definitions made about what is going to be accomplished and how that accomplishment is going to need to be done.

I have a tendency—there is no question that I am aware of among everyone concerned that there needs to be more information. I have a tendency to be a little leery when Government begins to further involve itself in establishing these things because there seems to be an effort to go overboard many times, go way beyond, and I am hopeful that we can make this as easily—as easy to comply with as possible and try to accomplish the goal without further complicating things, and I appreciated the comments that you made.

Dr. Burke, I believe it was in your testimony when you were talking about the survey and study that was done on 74 patients in a fairly unrealistic—who did the study or the survey that was done at that point that established the data that was used to, I presume, market the product?

Was it the company that was the manufacturer?

Dr. BURKE. It was a company-sponsored study. An independent investigator performed the study, a specialty surgeon, a urologist, and it was performed in a restricted population of long-term care patients with a heavy bias toward one gender of patient in that study.

Mr. COMBEST. OK.

Dr. Topol, you had mentioned in your comments, and I appreciate your mentioning it. I just want to reemphasize, the specific, two specific procedures or actually devices that are used are ones that I had made reference to earlier from a cardiologist in my district who is very familiar with your studies, writings, and obviously with the procedures, does not question the fact that the balloon method is, in most cases, much more usable.

He is concerned that in some instances, and went into some of those in medical terms, when he found that the Roto-Rooter approach was—actually was best to use, and his concern—I think you acknowledged that in some cases that is, in fact—that in terms of overall general practice and use, that it has not been as successful, but that he—his basic bottom line was that he would hope that whatever is done in an effort to provide more information did not result in the inability of having varieties of different devices or pro-

cedures available, because in some instances, he did find that they were much more successful.

Dr. TOPOL. I couldn't agree more with this point, that there is a place for the atherectomy, the new technology, but it isn't in nearly as broad an application as was envisioned, and so right now in the United States there is about 400,000 procedures done, nonsurgically, to deblock coronary arteries, and for there to be 60,000 atherectomies, for example, 15 percent of these procedures seems high, and I think our trial can really set some boundaries on this that it really does not—it might have evolved to be the procedure of choice otherwise if this trial had not been done in a timely fashion.

But there is absolutely no question that in select patients with the appropriate operators and judgment, it is an excellent technique, but it is not ready for the really broad use that was envisioned just a year or 2 ago.

Mr. COMBEST. And I want to make for certain that there is no misunderstanding that he has no disagreement with that whatsoever, with what you just said. His, again, basic bottom line was, I think, maybe being a little protective of this more than anything else, was to hope that the results of—particularly if we are determining procedures which seem to be, after studies and whatever, the most beneficial or the most realistic to go with, that that does not then result in, while maybe unintended, but that the reality of the result is not that there be a lack of other procedures or devices available and that just simply—I wanted to make that point, and I will yield back at this point so others can ask questions, Mr. Chairman.

Chairman WYDEN. I want to recognize my colleague from Massachusetts, but only say that—because as I understand what you all and people in the medical profession are saying, is knowledge and proof is the best defense.

What we are trying to do is get our hands on good comparative information so that in a sense, the physician, Mr. Combest and all the physicians I represent, Mr. Torkildsen, have more information so that they can make better choices, but choices that are grounded on a good scientific foundation, and then we can say, with solid scientific foundation and better proof, doctors are going to be in a more secure position as we debate a new system.

Gentleman from Massachusetts.

Mr. TORKILDSEN. Thank you, Mr. Chairman.

I again want to commend you for pulling together a panel of experts. I have certainly appreciated the testimony of each one this morning, and I will just go over a few points.

Dr. Topol, I think you were mentioning about the problem of flawed studies being used as advertising—tools and, granted, it is a major problem. Once a, quote, unquote "study" gets out there and it is used to promote sales of a drug, it is very difficult to track down how many decisions were made based on that flawed study.

Do you have any recommendations about how the medical community could rapidly get information? I guess this question could go to anyone on the panel, about disseminating information about studies that were not accurate, so that prescriptions are not made based on flawed information?

Is there some way to sort of catch that before it is put out on the wire?

Was it Dr. Burke?

Mr. TOPOL. I think that was Dr. Burke.

Mr. TORKILDSEN. Dr. Burke. Do you have any suggestions on that?

Dr. BURKE. I think the Chairman's proposal goes—it is the first proposal I am aware of that addresses this issue, and goes a long way toward solving it. I think we have to create an environment that is conducive to generating the kind of data from large numbers of patients in representative situations that are needed to answer the questions regarding medical devices.

It is very humbling to address this problem because of the vast array of different types of devices.

Currently, for example, one of the pressing issues is new devices for preventing needle stick injuries among health care workers. There must be dozens of these devices that are being evaluated and marketed, and it would be terribly inhibiting to innovation to anticipate some sort of clinical trial for each of these devices, and a randomized trial of each device would clearly be beyond the resources of our system, but we do need to find some way to facilitate the introduction and marketing of the most effective devices.

Mr. TORKILDSEN. Thank you. Dr. Avorn, my home and my district are just a few miles North of Brigham and Women's and Harvard Medical School and I certainly appreciate you taking some time to come here and testify.

Some of your comments are right on the mark about how can you expect a company who is—hopefully, I am remembering that you said these, a nine figure sum in research to really do a comparison with the lower cost alternative, and I guess that also hits upon what Dr. Marshall was talking about, how would even a company that produces a very low cost alternative invest money when they may not even see that they can recoup the cost of their study if their alternative is so low cost?

So any suggestions there on how that could be done? Could it only be done by the Government in your perspective or is there some other way to say, let's— and the cost factors involved in the study itself, I am sure, are there, but I am sure there are concerns about malpractice suits if certain techniques are not done as well, so that is part of the cost factor.

Do you see anything absent a pure Government role or is there some alternative that either of you see so that those studies and that information can be obtained?

Dr. MARSHALL. I would like to make a comment on that. With a new very cheap therapy or a therapy that could not usually make a large profit, the FDA, I think, does have a process called orphan drug development at the moment, but that is designed to be for a very, very expensive new drug in a small number of patients, and you need the same kind of mechanism for a very, very cheap type of drug in a large number of patients, and I see the suggestions by Mr. Wyden regarding special exclusivity for bringing out new usage, say, for a generic drug, such as triple therapy as we call it.

I would say that the length of the exclusivity should be linked somehow to the profit margin of the drug, and maybe when the

company has made 20 times its original investment, because there is a lot of risk involved with all of this investment, well, then the exclusivity kicks out at 3 years, or 20 times profit, or some formula like that.

For instance, then if the company brings the drug out very cheaply, well then they could expect longer exclusivity, whereas if they price gouged with it, then they would have to bring back all their profits in the first 3 years, which may be the way to go because after that time, it would then be accepted and generic and there would be competition back in the marketplace to bring the price way down.

Mr. TORKILDSEN. Thank you.

Dr. AVORN. If I could also comment on that. I think different kinds of situations are going to require different sorts of solutions, and the issues that you are raising, I think, are most appropriate for where there is inexpensive therapies that are probably never to going to make anybody very much money but are nonetheless, as Dr. Marshall indicated, potentially very, very important.

That is probably the kind of instance in which the Government ought to be involved, not to do the studies, but to support the studies, and the NIH model, I think, is a good one there; that a group of people with the public interest in mind thinks about what are the questions that need to be investigated, a request for applications is put out, and Government's role is to provide the resources for independent scientists around the country, peer reviewed, to do the work and then provide the answers to the medical community.

That would probably be the best way of dealing with the particular kinds of issues that you are raising.

Mr. TORKILDSEN. Thank you very much.

Dr. MARSHALL. That needs a different funding mechanism than the current NIH mechanism where, as you said, NIH is interested in basic research. If they want to—we want to clone ulcers or design a new antibiotic, NIH will support that, but if we just want to say, there is one on the shelf, let's test it, it doesn't give that very high priority, and clinical studies are languishing.

Therefore, I think that incentive to get private industry to get out there and be entrepreneurial with these new things is much more effective.

Mr. TORKILDSEN. A follow-up in a not entirely related question but in some ways it is because of the financial implications, the cost, per approval from the FDA is staggering.

I mean, so much money goes into research for drugs which are never approved.

Do any of you have any thoughts on what would be a fair mechanism to allow companies who do invest enormous amounts of money in research for drugs that are never approved, effectively companies now will sell drugs that are approved at a premium that will allow them to cover the research costs for research that never amounted to any, usable cure or drug?

Do you have any thoughts on that at all? Because I think that is something we are going to have to come to grips with in the future as well as price escalation is dictating a lot of our health care choices.

Dr. MARSHALL. I would say that bringing some cost consciousness into the FDA is going to help. Looking at this therapy, it is going to cost $20 million to evaluate that.

If there were potential and long-term goals, you could find sponsors to support that without any trouble. But if these studies have already been done in other countries, for whatever reason, and the drugs are already approved elsewhere, the FDA could perhaps give more weight to those other studies and perhaps look at cost-effectiveness of further duplication in this country.

I agree something should be done.

Finally, I would say that all the drug companies are terrified of upsetting the FDA. Therefore, the FDA does not get much constructive criticism. As far as I can say, from the drug companies or the manufacturers because, upsetting one person in the FDA could hold up an application and cost your company millions and millions of dollars.

So there needs to be sensitivity, I guess, from Congress because this is where the information percolates up from industry back to the FDA. It never goes straight from the person involved to the FDA. As far as they are concerned, everything the FDA says is gospel.

Mr. TORKILDSEN. Thank you very much, Mr. Chairman.

I yield back the balance of my time.

Chairman WYDEN. Thank the gentleman.

The gentleman from Texas.

Mr. COMBEST. Dr. Marshall, you made a great argument why FDA shouldn't be doing this. I don't know. One thing just came up.

Dr. Marshall, in your findings, do all of your peers agree with you?

Dr. MARSHALL. Yes. If they don't agree, they are not my peer.

Mr. COMBEST. I have got the same feeling.

Dr. MARSHALL. Let me say that this was—anybody who actually looked at it realized this was scientifically valid and effective and was—all the double blind studies in many countries showed the same things, but it took a long time to get accepted in the United States, and one of the reasons is that who is looking at these FDA grants?

They are senior physicians and gastroenterologists who are inherently very conservative, so that if you have a new idea that comes up, gastroenterologists probably have a vested interest in keeping all those ulcers ticking over, because they don't have to look for new patients after they have got 1,000 or so because the same ones are coming back every year.

So you have got to realize there are things in the system in the United States which make it inherently expensive and conservative, and they need to be looked at. It is not absolutely perfect.

Mr. COMBEST. My trying to assume why they might not, it would be safe to say that not everyone agrees? I am not trying to pick on you. I am just trying to get to a point.

Dr. MARSHALL. Well, we say that everybody who knows about it agrees.

Mr. COMBEST. I feel that way about a lot of things I introduce a lot of times.

Dr. MARSHALL. There is a NIH consensus conference to address this fact, that the therapies are out there, but at the moment, they don't have the stamp of approval and therefore they can't be advertised by the drug companies, and that will change.

Mr. COMBEST. The point I would like to make is that maybe everyone who does know in your instance, does agree and anyone who doesn't agree, doesn't know for sure, but I do know that there are, in a lot of treatments, or a lot of areas among experts who have tremendous backgrounds, there is disagreement, and I want to point out—the reason I want to point this out was that simply by having a monitoring body, whomever that body may be, FDA or anyone else, in an instance when the people in the field have disagreement looking at the same data, it may not be easy to come up with some of the—some suggestion about there being one product or one thing better than another where there is a large area of disagreement.

If there isn't a lot of disagreement, it would be quite simple.

I guess, again, I want to sort of put this on the record because it does concern me that while there may be lots of disagreement, we better know what the answer is before one starts making recommendations that can have huge implications, and I think that sort of goes back, Dr. Hillman, to what you were saying is that we had better establish the criteria by which we are going to judge things.

Thanks, Mr. Chairman.

Chairman WYDEN. I thank the gentleman.

Again, to come back to this matter of what comparative data is used for, as I understand it, you all want comparative data to get out to providers, doctors in the first instance, because all of this data is useful to them, and doctors don't look at this as picking winners and losers. That is what companies do. Companies are interested in the bottom line.

But as I understand it, what you all want to do is get data out to the provider, the physician in the first instance, ultimately to the consumer, because all of it is useful if it is of a comparative nature and well done; is that right?

Dr. AVORN. If we do believe in managed competition or in a marketplace for health care, you can't have any of those without adequate information on the part of the people making decisions, whether they are payers, doctors or patients, and I think it is very important to make the distinction between the availability of good information, which everyone is in favor of, versus what Mr. Combest seems to be rightfully concerned about, which is censorship.

We are saying, OK, now there is a body of people who have sat down in Washington and said you can't have this drug and everyone has got to use that drug. I don't think any of us is advocating that, unless it would turn out that there is something that is proven to be worthless, and that is what the FDA is about.

Many years ago there were people who said some folks like to use crushed up leaves to treat certain kinds of problems. Who is to say they are wrong? I think as a Nation, we have agreed that it is OK to say they are wrong if those approaches tend to be useless for everybody, and there will be some of those, but a lot of

them are going to be probably not the best way to go, but it may be relevant to some people.

The only way to know that, however, is also to generate more information, so you find out who are the 10 percent of people who are going to benefit from atherectomy or who are the 4 percent of people who may do better on this drug that is not the best drug for everybody.

Dr. BURKE. May I comment on that, Mr. Chairman?

It seems to me that so often in this problem, as in many others, we are addressing balance, and I think many of us could subscribe to trying to address an imbalance in the evaluation of drugs and devices that perhaps a bit too much emphasis is placed on evaluation before marketing in the sense of doing these small premarketing type studies and generating the type of studies that are required for FDA approval and too little may be done to evaluate drugs once they are out being used in large populations.

The phase four study emphasized by Brent James earlier in his testimony, to date, we really essentially rely on voluntary reporting of adverse events for post-marketing surveillance, but little is done to perform active studies in large population data bases.

Chairman WYDEN. Well, it is a very thoughtful point, Dr. Burke, because it is, in fact, a balancing issue.

If you have something that is promising that is going to save people's lives and also reduce costs, you do want to get it out fast, so you want to look at incentives for premarketing, but I think all of you have made a very persuasive case.

We want to focus on post-marketing. The proposal that I have been discussing certainly tries to do that as well, and I think it can be strengthened, given the concern we have got and the comments you are making.

Dr. TOPOL. Mr. Chairman, I just wonder if I could point out that there is no argument about the primacy of these clinical trials and meaningful data.

I think the real charge now is to get more of this in the future and how to organize a better, more favorable environment so that we will have large scale, meaningful trials, and one of the problems with the post-marketing approval—for example, in device technologies, is that you need to have an adequate number of experienced operators and you can't often achieve this in the premarketing phase, so that one idea was to set up a conditional approval format to go along with the points of your proposal, but also to be able to amplify the likelihood of meaningful data in large numbers, because one of the biggest problems we see are trials with small numbers of patients trying to make too broad or too sweeping a conclusion.

So one possibility to get those kind of meaningful and important findings would be from a mechanism that leads to conditional approval of a device technology with subsequent review after much larger numbers of patients have been studied in a meaningful fashion.

Chairman WYDEN. Well, an interesting idea, and I gather that we are going to hear from payers in a little bit that they are trying to fund that kind of thing as well. Let me—I have got some questions for all of you and this has just been a superb panel.

Let me start with you, Dr. Topol. I gather what you are really saying is that the principal activity of the Agency for Health Care Policy and Research, guideline development, is useful, but badly needs more scientific data to support it; is that correct?

Dr. TOPOL. Well, it is very much a situation, as we are all sitting around a table, and what do you think? Well, what do you think?

There is a rare occasion when you can cite, here is a randomized trial and data that supports this actual recommendation with hard data. So the agency practiced guidelines, which I think we are going to be relying on quite a bit over the next few years until we have better data to support recommendations, are quite subjective and it is very unfortunate.

Chairman WYDEN. Is there any data opposing or contradicting your trial of the atherectomy?

Dr. TOPOL. No. There is another Canadian trial which had the exact same findings in a smaller number of patients.

Chairman WYDEN. Let me ask you in terms again of sort of a logistics question we are going to be looking at as we discuss this proposal in the months ahead, could there be a role for the FDA advisory panel—I know you serve, I think, on one of them—with respect to approving the design of a manufacturer's proposed approach to doing a comparative clinical trial?

Could the advisory panels play a constructive role there, and again, possibly help hold down some of the costs here.

Dr. TOPOL. Yes, I think so. Until now, and still today, there is no interaction between advisory panels and the project plans for developing a new technology.

In fact, the only time we come into play is after the device has gotten through to the last phase of approval and then the advisory panel is brought in to determine whether or not the device technology warrants commercialization.

So getting earlier involvement, which I think was a strong recommendation from the Temple report, would be a very favorable positive thing.

Chairman WYDEN. We are going to want to ask you for your input on that as we go along because clearly that would be one way to get both academic and industry input.

Those advisory panels, I think we look to health reform, can play a very constructive role and your involvement there would be very helpful.

Let me ask you a question about the atherectomy that is a little bit unrelated to what we are talking about, but since we have you here, it would be helpful to have your thoughts on it.

The subcommittee has picked up some evidence that in the case of the atherectomy, the trial data used to get the device approved was produced by scientists who had a stake in the company manufacturing the device.

Are you at all concerned that the data that is obtained on some of these new devices not only is not comparable, as we have been talking about today, but is also being produced by individuals with a stake in the product's success that could color how it is handled?

Dr. TOPOL. I don't think that really was an issue, but I—because I think no matter what, it is always a company that is involved in these new technologies.

So if it isn't randomized, there is just no validated set of data to draw from. So I don't believe, in the case where there was both the company and an inventor involved in bringing along the technology, that was the problem, but more so it was just lack of controlled data.

Chairman WYDEN. Let me move on to you, Dr. Burke.

The FDA hopes to protect individuals by limiting manufacturing claims to approved labeling indications. This generally doesn't permit cost-effectiveness and superiority claims.

Is the net effect of this policy to protect people, and how can you balance these seemingly conflicting goals?

Dr. BURKE. I think informally, many representatives of industry would recognize that the largest profits come from the sale of the drug for nonapproved indications.

Many of our broad spectrum antibiotics are a case in point. They are primarily used because of the doctor's fear of what the patient may have rather than because of what the patient in fact has and what the drugs were tested for in preclinical evaluation.

One of those broad spectrum antibiotics is a good example of this. This drug was found to be safe and effective in virtually all the preclinical testing, and it wasn't until it was used in large numbers of patients in—virtually throughout the United States that it was recognized to be a significant cause of bleeding and caused much more bleeding than any other of some very similar antibiotic compounds.

So I think what this emphasizes is the importance that even a study that is randomized is not always adequate. My example of 74 patients in the catheter study was—happened to be a randomized study. It just simply didn't address the right population.

Chairman WYDEN. Do our other panelists agree with this point Dr. Burke is making? Dr. Topol does, Dr. Burke does, and Dr. Avorn does.

Dr. Hillman, are you of undecided mind on this?

Dr. HILLMAN. I am embarrassed to ask you to restate it in a little bit more succinct way.

Dr. BURKE. It seems to me that the—a new medical device or a new drug that is being evaluated has to be evaluated in all the uses to which it is put, not just in the uses for which it is originally designed and tested.

Dr. HILLMAN. Yes. I think that is—that is asking the impossible because which comes first, the chicken or the egg?

We approve a drug based on very narrow testing in the FDA. It goes out into wide use. It is used for other purposes and then other purposes are tested. Then the test results come out. So to say that it has to be tested in every situation in which it could possibly be used before it is used, I think is unrealistic.

Dr. BURKE. Absolutely. But if my species does not survive to do those testings after the drug is in use, we won't have those comparative evaluations.

Dr. HILLMAN. I don't want to put your species out of—into extinction, believe me, but I just want to help the committee come up with a practical and realistic policy so that we can have the absolutely necessary randomized controlled clinical trials we all agree are necessary and the balance of controlled clinical trials with post-

marketing testing in a way that the pharmaceutical companies and the device manufacturers can use so that they have the incentive to use that information.

I think it is really crucial that the committee understands that the companies that do this work cannot use it in their marketing efforts and therefore there is no incentive to do so.

Chairman WYDEN. I think what Dr. Burke is saying and what I anticipated everybody agreeing on before we went to a debate before that I am still trying to track, is that what Dr. Burke is saying, most of the money is made on the nonapproved indications; is that correct?

Dr. BURKE. Yes, that is right.

Dr. AVORN. Mr. Chairman, there is one important point that came up in the debate I want to clarify because I don't think my colleagues on either side of me really disagree.

I think it is important to distinguish between data that ought to be available in order for a drug to be licensed by FDA, and that is the narrow control trial kind of information, and then there is the data that we need to go on collecting after the drug has been approved for use, which can happen afterwards.

I don't think anybody would like to demand that the comparative post-marketing surveillance data occur before the drug is made available to the public.

First of all, you couldn't do it and I don't think anybody would really want to. FDA unfortunately right now just has kind of an all or none approach in that a drug is either denied registration or it is made available and then that is the end of the inquiry.

It is like a legal system that either had capital punishment or nothing, and drugs either get killed or they can go scot-free, and I think we need something in between. Probation, I guess.

Dr. MARSHALL. I would like to comment on a nonapproved use, and the example is Tagament which came out in 1978 and was approved for the treatment of ulcers. It is easy to show that things work with duodenal ulcers because they are so common and you can easily heal them.

So Tagament came out and was approved for use in duodenal ulcer, but it was not until 1984 or 1985 that there was actually a double-blind study showing that it was effective for gastric ulcer.

But common sense would indicate that it would be effective for gastric ulcer since antacids, everything else for duodenal ulcer is for the gastric ulcer.

So that it would have been unreasonable to deny Tagament for the treatment of gastric ulcer in all those people who didn't really have any better thing to use between 1978 and 1984, 1985.

So I agree that this needs—it is a two-edged sword and if you get more restrictive, you will lose interesting new opportunities or interesting new uses for a drug that wouldn't have come to light.

Chairman WYDEN. The only other question I had for you, Dr. Burke, it seems to me that you all have really been out in front in terms of integrating quality improvement with comparative effectiveness research.

I mean, that is really the name of the game is to put those two together. Clearly I am interested in trying to come up with some

irresistible incentives to the companies to try to make them want to come forward.

The Clinton administration has other proposals on quality improvement. What ideas might you have on how these two concepts could be integrated?

Dr. BURKE. I am not sure that I can succinctly state that for the Clinton administration. One would hesitate to suggest the creation of a new Government agency, but clearly I think the focus of the Agency for Health Care Policy and Research in my eyes, in the eyes of many investigators, would be better served by sponsoring clinical research to answer some of these questions than by—than purely through practice guideline development, or only through guideline development.

I think the notion of having inducements for companies to sponsor research is clearly valuable. We don't need further post-marketing surveillance on penicillin G. That has been around for 40 years, but there may be a period of time, of 3 to 5 years after a new drug or device is introduced, when conditional approval and intense surveillance in specific sites is warranted.

Chairman WYDEN. What exactly is your understanding? As five practitioners in this field who have spent lots of time thinking through these various kinds of issues, what is your understanding as to what the Agency for Health Care Policy and Research is doing with respect to comparative clinical research?

Are they doing some? Are they doing——

Dr. AVORN. Very, very, very little, and having spoken about this with people at AHCPR who I have high regard for, I can tell you what their view of it is. That is that their budget is so tiny and they are so daunted by what it costs to do adequate clinical trials, that they feel that they would be swallowed up and there would be nothing left if they got into this area, and so they shy away very, very fearfully from funding this kind of work.

Chairman WYDEN. Any others? Anyone disagree with that point?

I think it is really unbelievable that this agency, this itty-bitty agency which we want to be doing some of the most important possible work in health care can't even make a beginning in terms of addressing what you all are talking about, because as I go around the country and I talk to buyers, health maintenance organizations, insurance companies, individual providers, people are hungry for this information and then they usually say, well, Ron, I heard this was this little agency back in Washington that is supposed to be doing it, and I guessed somehow outcomes effectiveness analysis is going to kind of pour from this little agency and we will get it, but it is very obvious that we are not and it sure undermines, as Dr. Avorn has said, this whole idea about how you make managed competition in the system work.

In fact, every one of the proposals, whether you are a single payer person or from Medisave or anything else, is really built around the idea of trying to get better information to make solid health care choices, and what you all are basically saying is the emperor doesn't have any clothes.

There is an agency that ought to be trying to get this information out, and I think even fairly well-informed people, Mr. Schulke, I think, knows about as much about this issue as anybody in Amer-

ica, and he just whispered to me, let us try to find out exactly what the practitioners in the field think is taking place there, and our understanding was that there was some, and we will be discussing this with them some more, but——

Dr. HILLMAN. Mr. Chairman? I think it might be important to point out that one of the emperors also has his winter coat on during the summer, which is the FDA, and the very kind of research that you want to incentivize and the incentives that you will use to bring that research to bear and to have more of it will not be able to be used in the marketplace under current law, and if we are talking about free market and we are talking about managed competition, I completely agree with Dr. Avorn's point.

We have to create a system where we not only create the information, but we allow the people who create the information to use it and the doctors and the buyers in the field to avail themselves of it.

Chairman WYDEN. Well, I share your view and I think Dr. Kessler does as well.

I have talked to him about this, discussed these ideas with him even yesterday, and I think that he, in this recent initiative they have taken, is a step toward trying to change the system, and that is why we want to use the appropriate and relevant trained national health reform when people, if anything, are going to need more information to try, as you say, whether it is the Emperor doesn't have any clothes or wearing the wrong coat or something like something else, we don't disagree with respect to the dire need to try to address this and get good information out.

Let me turn to you, Dr. Avorn, for a minute. You have been out there in the vineyards slugging away at the need for better clinical data for doctors for a lot of years, and I remember back in the days when I was co-director of the Great Panthers they were talking about the kind of work that you and your association were doing before John Heinz' committee.

Have the drug companies done enough to include seniors in clinical trials and in general to make clinical trials reflect the real patient population that is eventually going to use a product?

Dr. AVORN. I think they haven't yet done so. There are some labeling requirements that have been floated by FDA years ago which have not really yet been implemented to indicate how drugs ought to be used in the elderly.

There are some classic examples of drugs that are used mostly by old people in which the labeling contains information about—and these are heart medicines, use in pregnant women, use in nursing mothers, use in children, and there is not something about use in the elderly.

That really does need to improve and we still have an under representation, not of the 65- to 70-year olds; they have begun to creep in, but we have a real underrepresentation of the old-old and of people who are complicated old people who we need to know about how these drugs work in them because they are the ones who take a lot of these drugs.

Chairman WYDEN. What do you think about the concept of using extended exclusivity to get manufacturers to particularly look at

the targeted populations, say the seniors, the kids, at-risk minority populations, those kinds of groups?

Dr. AVORN. I think as with the comparative study, which is the other purpose to which you are proposing, it is a very good approach as one of three, and I would like to just mention the other two.

As I see it, one can get better data out there if we are talking about the drug industry and we can come back to the payers in a couple of minutes, but the industry I think can be addressed either with carrots, with sticks, or through the marketplace, and probably all three need to happen.

You have very eloquently described the carrot approach in which there is something in it for them and there is something to be said for encouraging the industry to do that which it can do well, and perhaps that will make it do less of some of the less helpful things that it has done in terms of me-too drugs that we don't really need.

So I think in that sense it is a step forward.

The stick approach would be to say, gee, this really is something that they ought to be doing anyway; let's just make this part of the drug approval process. That is politically much more difficult and therefore may not be as viable as what you have proposed.

But I do think we can tighten up what FDA does expect of manufacturers in terms of what they are comparing their drug to, who may study it and so forth, at the same time that we are growing our carrots.

Then the third approach, which is not exclusive of either of the other two but is probably also something that ought to go forward, is the marketplace in which I would like to think that in a couple of years, big buyers of drugs, whether they be HMO's or insurance companies or whoever, will look critically at the data that are out there and it will behoove the industry to have generated data about comparative efficacy vis-a-vis other drugs, about cost-effectiveness, about use in the elderly, because I would like to think that HMO's in 1998 will say, we simply don't want to add this drug to our formula because the manufacturer has not caused there to be the data that we like to see about its cost-effectiveness or any of the other variables that we talked about.

So I think all three need to go forward, the carrot, the stick, and the marketplace.

Chairman WYDEN. What are the major conclusions of the expert panel you convened on medications in the elderly that Congress ought to be taking into account now as, again, the focus has turned to a Medicare drug benefit?

Dr. AVORN. Certainly the ante is upped by virtue of the fact that the Nation may well be paying for the drugs for the elderly very soon in large volume.

This was a group in which we were fortunate enough to have David Schulke as a member and so we had representation through David and others of Government, of industry, of academia, of practitioners, and there were a number of issues that I think I can summarize very quickly.

First, is that we do need to know more about how drugs work in the elderly, and saying that people under 70 are elderly in this regard is not adequate.

Second, we need to understand much more about how drug utilization review ought to go forward in the elderly, and there is a lot of simple-minded computer programs out there that may or may not do any good. They screen large numbers of prescriptions and say this is good, this is not good.

There needs to be great development of the clinical intelligence behind many of those programs moving them in the direction that I think Dr. Burke and his colleagues in Salt Lake would like us to move to instead of rather simplistic approaches.

In addition, I think we need to find out more about how medications can be used to prevent more costly outcomes in the elderly. There is this fear that if we are spending a lot of money on drugs, it is all money that is kind of gone.

In many respects that may be some of the most cost-effective dollars that we spend and we need to understand more about that rather than just looking at what a drug's price tag is.

Chairman WYDEN. Let me ask you one other question again on this conflict of interest issue that I started touching on with Dr. Topol.

According to recent testimony before a FDA special panel, Ms. Carol Scheman, the deputy commissioner, said that only one-third of all applications before the biologics and device division, and I quote, "have investigators who have some sort of interest in the product that is the object of the evaluation process."

Do you have a concern about this? If so, do you think that there is a need for more public disclosure? What would be your views on that?

Dr. AVORN. OK, I think disclosure is always a good idea and it may be all we need in this regard in that the people who develop a new technology, and this is perhaps more relevant to devices, maybe also biotechnology, are likely to be the ones who are going to be the first people who study it.

I don't see any way that that is not going to happen, but there are a couple of very specific things that I think can protect the Nation against any kind of problems and scientific misconduct.

One is absolute disclosure of all potential conflicts, and at my medical school, that is something which is taken very seriously and every year we need to complete forms about any connections with the private sector.

Second, I think Dr. Hillman has moved things forward in the stretch, is very clear ground rules about how studies get to be designed, how data are going to be analyzed, how reports are written, who gets to see the reports, who gets to comment on them, who gets to publish what they want, and if there are sort of a Helsinki Accords kind of approach, that these are rules that everybody signs off on, that can make it possible for these very often talented investigators to be part of the process, but will make it also possible for the findings not to be distorted even unintentionally.

The other antidote that is worth mentioning is that if there is support that is available from a nonprivate source, i.e., the Government, that makes it a lot easier for an investigator to be able to pursue his own way and not worry about what the sponsor is looking for.

Chairman WYDEN. Dr. Avorn, you have been very helpful and we are going to be asking a lot of you in the months ahead as we try to shape this proposal.

Let me move to you, Dr. Hillman, if I could, as we have been talking about. I am looking at a proposal mechanism to make it attractive to companies to conduct these comparative studies and then brave the FDA approval process for supplemental labeling.

Do you think that this concept, this proposal, is one that makes some sense and that you feel, as we refine the definitions and the concepts, is one that is attractive?

Dr. HILLMAN. Yes, I do. I very much support the spirit of the proposal. I think it will accelerate a direction that we are going, which is the pharmaceutical companies and the device manufacturers responding to the marketplace demands, as Dr. Avorn and others have mentioned.

But, again, and not to beat a dead horse, I think that, the horse is dying, but I will make the point once more, it is absolutely irrational to sponsor this kind of research, to offer incentives, and then not to allow the companies to use it or not to allow people to use this information.

So I think that the spirit of the intent of the legislation is excellent, but it has to be more comprehensive of the big picture in order to have its effect, and I am sure that you will refine it in the coming weeks.

Chairman WYDEN. Do you believe that drug and device companies should be allowed to use published data from clinical trials that they didn't themselves conduct under FDA supervision?

Dr. HILLMAN. In marketing materials or——

Chairman WYDEN. Yes, marketing.

Dr. HILLMAN. Yes, as long as it is conducted under the traditions of scientific peer review and good research.

Chairman WYDEN. Those would be the standards, that it would be peer-driven and peer-reviewed?

Dr. HILLMAN. Those would be some of the standards. In the article that I wrote, we set forth nine standards, and in the task force that we are convening, we are trying to refine those and group them, but I think that most of the—or all of the basic standards of basic scientific research apply to this area, but we need some other things as well because effectiveness research by its very nature is more malleable, less standardized than controlled clinical trials.

There is a 30-year history of how to do a controlled clinical trial and people know—I think a lot more people know a lot more quickly what is a good one and what is a bad one.

In a trial of effectiveness, there is a lot of information that can be interpreted, subject to assumptions, and this is the reason why we need a specific set of voluntary guidelines for that kind of research.

Chairman WYDEN. We especially want to work with you on this point because I think your idea makes sense. In fact, what we have been looking at is an idea to let companies use it even earlier as long as it was in line with the kind of standards we have been talking about in the proposal.

Now, you make of course the point about encouraging companies to conduct effectiveness trials after approval. We have got a couple of ideas that we wanted to ask you about in terms of kind of further refinements of what we are looking at.

What about the idea of giving varying license of extended exclusivity to companies depending on how early they complete approved trials?

Dr. HILLMAN. In general, I think that is a good idea, but I don't think that should be the only variable on which you decide the length of exclusivity because you could have a very unimportant drug on which you do effectiveness work that finishes very early, and then you are rewarding a company for producing a fairly unimportant drug with—just on the basis of how quickly it can get its research done.

So I think that there are other variables that need to be taken into account as well, such as the cost-effectiveness and the import and number of people it affects and the—whether it is a groundbreaking drug or a—what we call a me-too drug and various other types of variables.

Chairman WYDEN. I think our hope is that is what the study would show. So you overall would say that the concept is one that would make sense in conjunction with these other considerations?

Dr. HILLMAN. Yes.

Chairman WYDEN. What are your thoughts on the matter I asked Dr. Avorn about with respect to premarket clinical trials and exclusivity so that we could get more data about some of the target populations, elderly, kids, at-risk minorities?

Dr. HILLMAN. Yes, I agree with Dr. Avorn's very articulate points and I think that, again, the marketplace will start to require some of this information, but some of the special populations will not be addressed simply by marketplace forces because they are not big enough or they are not a big enough market or they are—or their insurance doesn't pay for it or whatever, and that is where perhaps some regulatory agency should step in with incentives like you are talking about in order to bring out the kinds of research in those areas that the marketplace would not otherwise bring to bear.

Chairman WYDEN. Let me ask you just two others. I have mentioned the FDA prohibiting drug and device manufacturers from using the comparative effectiveness information.

Is it not the case that these studies present the best possible case and not the real world?

Dr. HILLMAN. Which studies?

Chairman WYDEN. Well, these additional studies. I mean, it is no secret that the scientific protocols used to study new products prospectively clearly don't reflect the best practice of medicine.

So it would be our interest in knowing whether it is not the case that these studies present the best possible case, not the real world.

Dr. HILLMAN. Well, I think it is best and worst. I think it is actual and make believe. I think controlled clinical trials—and I am not arguing against the need for them. I want to make that perfectly clear.

They are, of course, essential, but they are not the real world and actual clinical practice, and an example that was given by Dr. Mar-

shall where, the H2 blockers were first approved only for duodenal ulcers in a very select population, but rapidly started to be used by almost everybody for everything is a good example, and I think that if you go out and you do what we call nonprotocol driven trials, you just observe and you look and you see how things are being used in the actual clinical environment, that you are testing their use in real life.

A simple example is a drug that is taken four times a day and works beautifully in a controlled clinical trial because the patients are called by nurse-clinician monitors who say, did you take your pill. Then they call back 3 hours later and say, did you take your next pill? This is not the real world.

In the real world, you get a four times a day prescription and you maybe remember to take it once when you wake up and you might remember to take it once when you go to sleep, and you don't get the blood levels. You don't get the blood levels to kill the infection that you have, and therefore the antibiotic doesn't work in the real world like it worked in the clinical trial, which will, of course, impact its cost effectiveness and that is what we really want to know.

Chairman WYDEN. Now, all physicians do not medically treat the same patient the same way, and as you know, we were talking about variations in medical practice and these obviously can present a difficult variable to factor into any study on reducing cost.

Can you offer us any suggestions about how we can make sense of cost-effectiveness information from controlled studies when standards of practice seem to add this wild card variable that is hard to control?

Dr. HILLMAN. Yes. I think that is a critical question because in my written testimony, I made the point that we don't want to overlook the opportunity to try to reconstruct effectiveness information out of preclinical studies, and the way to do that, the way that we have had the most success in my group at Penn at least is to convene a panel of experts to tell us how the protocol-driven preclinical approval studies differ from actual clinical practice, and run simulations to determine whether we would get a different answer if they had been done under different circumstances.

So my whole testimony here is not to say that preclinical studies are useful. It is just to say that special care has to be taken to get the appropriate information out of them.

Chairman WYDEN. We are going to want to work very closely with you, and I want it understood that what we have here is work in progress.

Your point earlier that we have come back to trying to define some standards is absolutely key. I mean, this is a voluntary concept.

Dr. Avorn was talking about carrots, and as such, I mean, the worst thing that is likely to happen is probably nobody does it. They just don't find the carrots attractive, and then we don't get about the task of getting more comparative data and don't have all the opportunities for using it throughout the many stops in the new system, whether it be alliances or the Agency for Health Care Policy and Research.

So we are going to work closely with you on this matter of trying to define the terms and making them ones that work in the real world on both sides of the equation, early on in the premarket days, and also to reflect the post-marketing situation.

Dr. HILLMAN. Good. Well, we welcome that and we also use many of the same terms as you do in your last point, at least in your letter to me, was that you were thinking about kind of a Federal seal of approval of some kind, and we are hoping that the guidelines that we come up with could be ignored, as you said, and companies can take the risks of doing trials in a different way, but if they did submit to the kinds of guidelines that we are coming up with, that they would have the seal of approval of at least having claim to following our guidelines.

Chairman WYDEN. The one kind of tool here, of course, that is why I am very interested in seeing what you are talking about in this network of biotechnology companies, that at some point, savvy buyers might insist on this kind of information given voluntarily.

In other words, we have got a situation with, if we make this part of national health reform and somebody who is running a biotech company in my district or Mr. Torkildsen's or any of my colleagues says, nuts on this, what Ron Wyden thought up is just a bunch of eye wash, I am not going to do it, I am going the regular route, they could still do that. There is not going to be anything that bars them.

But what we hope to cultivate is a kind of new ethic about medical technology information where buyers are going to say, shoot, if you are really going to offer me something that is going to make a difference, you would have voluntarily gone into the process.

That is why we are going to ask you about it, and eventually buyers and physicians, hopefully one day consumers, can get this information more readily.

How soon do you think you all might have your voluntary guidelines fleshed out in terms of this comparative analysis project?

Dr. HILLMAN. We are scheduled to have them finished in the early fall of next year, and there has been a lot of up-front work, and we are already on schedule, halfway through the meetings we are supposed to have, so everybody may laugh at academic timetables, but I think we will be pretty close to that.

Chairman WYDEN. If you can come in a few months earlier, it would be very instructive because this Congress is going to enact, in my view—a national health reform bill will probably be added in terms of the health committee early next year.

Dr. HILLMAN. Just that remark may help me to goose my colleagues to coming in early.

Chairman WYDEN. It is important work, as you have heard me say. I think this is as important as anything else.

In fact, my sense is that the biggest concern is if we do not figure out a way to do this and get access to good comparative information, the real prospect is that Congress goes forward with national health reform legislation, all the members huff and puff and cast all these horrendously difficult votes, politically difficult votes, and votes that produce all these wrenching changes.

You get a new system in place and then a year-and-a-half down the road everybody says, what do we do next? Because you have

not gotten at these underlying kind of issues that you all are talking about.

So tell them forthwith they can speed up the timetable.

Dr. Marshall, for the record, we wanted to note that Sir James Black won the Nobel Prize for inventing the first of the H2 blocking drugs to treat ulcers. We would like to think that the person who discovered the underlying disease process and documented the superior and more cost-effective treatment for it might actually get a similar kind of honor today, and we are glad to be able to have you presenting your information. It was very helpful.

So I had a sense in terms of the numbers you would say on the basis of the analyses you did with respect to an alternative clinical outcome, that the findings you arrived at could reduce American health spending by $10 billion over 5 years?

Dr. MARSHALL. Yes.

Chairman WYDEN. A lot of money in my world.

Dr. MARSHALL. The problem is you could have worked that out in 1989, 1988, 1987, and because it was a new thing which was going against current dogma, it was not—it was probably not given as fair a go, maybe because it wasn't discovered initially in the United States.

Although in fact it was discovered in 1940 in Harvard by Dr. Freeburg who, at that time, the big high-technology medical thing was insulin for diabetes and he changed over to diabetes research and left the other research alone after that time.

Could I make a comment regarding the vested interest question for devices and products? I hold several patents and my feeling has always been that if I have got a good product, which is the cheapest product out there, or second best product but so much cheaper that it is cost-effective, I should be able to get it out into the marketplace and sold properly, and nobody knows more about that product than me, so that it is logical—it is logical that I would be involved in the initial clinical trial.

But I think the FDA does oversee these things carefully, and our role—our mechanism has always been to get other uninterested third parties into such an evaluation.

For instance, the FDA will always say, well, give us two studies in the United States and one study overseas or three studies in the United States, and it is important to get an uninterested, unbiased third party as one of your investigators, and the other protection is to get an unbiased—like a medical research company or drug research company to supervise the study and make sure the blindedness is correct and everybody plays by the rules.

I think anybody with any common sense would want to do that because it would be a terrible thing to have a product with an investigator that was biased and good out there, and then found to be an unproven or ineffective product, like recently the brouhaha we saw about these catheters that were breaking off by the Bod Company, so you wouldn't want that to have the worst possible outcome, and a prudent businessman would not allow that to happen.

So there are checks and balances in the system now. I have got no complaints about the way it is carried out in the United States really.

Chairman WYDEN. Let me ask you one other question, Dr. Marshall.

With respect to consensus conferences and particularly how they change physician practices, I guess there was an article in yesterday's Journal of the American Medical Association talking about, again, high blood pressure medicines and how the consensus conferences didn't seem to have much effect on changing physician practices in that area.

Is it your sense that this kind of tool, because certainly these consensus conferences are a way to bring people together, these kinds of conferences could be enhanced as well by the kind of comparative data analysis that we are talking about, could they not?

Dr. MARSHALL. That is true. The FDA has got obviously strict rulings and I think the good thing about it, everybody plays by the rules, and if you start first, you can expect to come out the front end first if you have got a new therapy, but there are other less restrictive types of data that are available, cheaper data that is out there, rather than the typical placebo controlled study.

As soon as you put placebos into any kind of a study, that means some of your patients aren't getting the treatment and it is hard to recruit. So there are other ways that you can get this kind of data.

The thing that the consensus panel puts an official stamp of approval on a product perhaps allows the manufacturer to create a product label which is approved by the FDA and therefore protects him from the liability which he would otherwise be carrying if he was trying to market a product which was decidedly experimental or untested.

Chairman WYDEN. Why don't the doctors now look to these kinds of sources?

Dr. MARSHALL. In the United States——

Chairman WYDEN. It is probably like the guideline development up at the Agency for Health Care Policy and Research. I mean, you got a number of these tools and they don't seem to be used much.

Dr. MARSHALL. Well, doctors obtain information about new drugs from the drug detailers, and so they will not change their practice until someone comes in, they receive a pen with a new drug written on it, maybe a little plastic spine if it is an arthritis drug which sits on their desks and something about indications and side effects and the results of a clinical trial, and the drug rep can get in and explain this to the doctor and he says, well, that sounds reasonable, and, here, I have a box of free samples, would you like to then start my patients on it?

So that works very well, and yet if you don't have the indication and if the NIH consensus conference comes out and describes a new therapy but there is nobody to actually get it out there in the marketplace and really push it, it just won't happen in the United States, but the good thing is when it does get to that stage of having a sponsor, it happens overnight in the United States and suddenly a new more effective therapy will be used by everybody.

So that it takes longer to get there, but usually the outcome is beneficial, but perhaps it could be speeded up some way.

Chairman WYDEN. Do others of you believe that there is this breakdown between the NIH consensus conference and the physician in the field?

Dr. AVORN. Absolutely. What is striking about the paper you are referring to is that we found something similar. Dr. Moynanen in my group and I have tracked the use of high blood pressure medications in the elderly over the last decade. Virtually every time there is a new study that comes out saying thiazides are a good way to beat high blood pressure in the elderly, the use of thiazides goes down a little bit more. Not up, but down.

The reason is that during this time a lot of other products, which frankly have been less well tested in the elderly, have been very, very heavily marketed by the industry. Nobody is really making any money off the thiazides anymore. There are the drugs I was referring to that cost $10 a year, so there is not a lot of capital behind the thiazides to get that message across.

The good news may be that thus far, although there has been really nobody's interest in getting these messsages about old cheap drugs out there and so we see this perverse direction happen opposite what of the research is showing, what we may be seeing in the next couple of years is that as payers get into the act, they will at least have perhaps a countervailing voice to the manufacturers who are very good at presenting the virtues of the new products.

We haven't had anybody very good at presenting the virtues of the old products, but we may begin to see a little bit of a balance in that regard.

Dr. HILLMAN. Just very briefly, I absolutely agree with that and I think, just to add on that, I think it is very important that the committee understands that the situation that Dr. Marshall correctly identified of the detailing in the doctor's office is going to change very quickly as we move into a managed care/managed competition or any other kind of environment.

The drug companies are already dismantling that drug detailing apparatus and gearing up and training people to deal with representatives of large purchasers—managed care buyers, hospital buyers or whatever—and these people have to be much more sophisticated people who understand comparative trials and effectiveness research and have to be able to make a case, and a pen or a little skeleton on the desk is not going to make the sale.

So although that is currently the modus operandi, I think that is going to change quickly and there will be hopefully more involvement of, consensus panels and treatment guidelines translated down to the local level, although right now, I think Jerry is absolutely right.

Chairman WYDEN. The drug detailee or whoever performs that function is basically going to have to make sense to the people on the next panel, who are essentially the buyers.

You are correct, it is going to be a different world and one would assume that these state-of-the-art kinds of mergers and the like, MedCo-Merke kinds of mergers, are going to focus on just that kind of information that you have pointed out.

You all have been very helpful and let me see if minority counsel has any questions.

Mr. LEHMAN. Just one quick question if you would.

Chairman WYDEN. Mr. Lehman.

Mr. LEHMAN. My boss had wanted to ask one further question. Dr. Hillman, you had mentioned that the task force you are on or in some work you are doing is funded partially by drug companies, so what you are saying is that they are beginning to understand and there is certainly a clear understanding on their part or in the marketplace that this kind of data can be useful to them. Is that what you are saying?

Dr. HILLMAN. Absolutely. There is a subset of companies who understand the horizon and what is coming and want this science to be launched in the most scientifically valid way. They have given no holds barred, meaning, they have given the money to the University of Pennsylvania to conduct this task force in any way we see fit as unbiased as possible.

So I think that the industry as a whole is coming around. The sponsors in particular are coming around faster. But the short answer to your question is, yes, they are starting to see the light.

Mr. LEHMAN. But there needs to be more done.

Dr. HILLMAN. There needs to be more done. But they are starting to see the light about the importance of this kind of research because of the marketplace.

Chairman WYDEN. Gentlemen, you all have been very helpful. We are going to be anxious to talk with you frequently in the days and months ahead, and we thank you for your cooperation and assistance.

Chairman WYDEN. Our next panel involves cooperative technology evaluations by Blue Cross and Blue Shield. Susan Gleeson, executive director, Medical and Quality Management of Blue Cross/Blue Shield Association in Chicago. Kim Quesnel—I hope I am pronouncing that correctly—R.N., manager, Medical Review and Utilization Review of Blue Cross of Minnesota.

I want to thank both of you for your patience. I know it has been a long, long morning and you all have been very kind to sit through it all. We are going to make your prepared remarks a part of the hearing record. We would like to ask you to summarize your major views in about 5 minutes, and it has been the practice of our subcommittee to swear all the witnesses. Do either of you have any objection to being sworn as witnesses today?

[Witnesses sworn.]

Chairman WYDEN. Ms. Quesnel, am I pronouncing your name right?

Ms. QUESNEL. Quesnel is correct.

Chairman WYDEN. Thank you again, both of you, for your patience. Why don't we begin with you Ms. Gleeson

TESTIMONY OF SUSAN GLEESON, EXECUTIVE DIRECTOR, MEDICAL AND QUALITY MANAGEMENT, BLUE CROSS/BLUE SHIELD ASSOCIATION

Ms. GLEESON. Thank you, Mr. Chairman, members of the committee. I am Susan Gleeson. I am the executive director of Medical and Quality Management for the Blue Cross and Blue Shield Association. I am very pleased to be here today to address this issue of clinical research.

Clinical research is a critical issue. It is one of the basic building stones needed in the reform; and if we don't have more and better clinical research, we are not going to reach the goals of health care reform. Those being the goals of universal access, cost management, and better quality.

Today I would like to touch on three areas. I would like to tell you about our technology evaluation program. I would like to tell you about our demonstration project in which we are funding the collection of comparative data. Third, I would like to make some recommendations on how we can improve both the quality and cost of the clinical research.

Let me start with our technology evaluation program. The association is the coordinating agency for 69 Blue Cross and Blue Shield plans. They are all nonprofit. They are self-governed and as a system they represent the oldest and the largest health care insurer. We insure over 67 million Americans.

Chairman WYDEN. So you all are engaged in the research function for the entire Blue Cross/Blue Shield network?

Ms. GLEESON. That is correct.

Chairman WYDEN. There are no Blue Cross programs outside yours for purposes of clinical research.

Ms. GLEESON. Right. We have major——

Chairman WYDEN. Blue Cross in Oregon and Blue Cross in Texas, they would all be part of your network?

Ms. GLEESON. They are all part of our network and basically I think a way to think about this function is we are the central resource that provides the information to the plans so they can make their business decision.

We conduct a technology evaluation program. We use a set of five criterion. What we demand is that there be evidence about the technology. The evidence must show that it improves the net health outcome. It must demonstrate that these outcomes outweigh the harms. That they are at least as beneficial as the existing alternatives which relates to your comparative trials.

We have been doing this work since 1985. We have done over 200 assessments and last month we made some major changes that I would like to brief the committee on.

First, we are now collaborating with Kaiser Permanente so we are pooling our resources and will now double our capacity. Every year we do 20 assessments. Next year we will be doing 40.

Also we have expanded our medical advisory panel. This is our physician panel that reviews the research. We have major technologies assessments methodologists on the panel. Dr. David Eddey is our leading scientific advisor. We also have technology assessment experts from Stanford, Harvard, and Johns Hopkins. We have expert clinicians who contribute to our panel. We have appointees from the American college of physicians, American Academy of Pediatricians and the American Academy of Family Practice. We also have leading oncologists. We have an ethicist and we have a consumer representative.

Finally, and I think it is in keeping with what has been talked about in the hearing is starting in 1994, our technology assessments which have been proprietary to the Blue Cross/Blue Shield system will now be made available to any interested party. We con-

sider these scientific information. There is a need for our purchasers and payers to have this information. There is a need for consumers to have it and also for physicians.

Now, through our work with our technology evaluation program, we got involved in our demonstration project for breast cancer. Breast cancer, as you know, is a very prevalent disease in women. One out of nine women have breast cancer and in the advanced stages we have very poor treatment.

In the late 1980's, researchers were advocating high doses of chemotherapy combined with autologous bone marrow transplant, which I will refer to as ABMT. We were familiar with this combined therapy. We had used it. We had evaluated it for leukemia and non-Hodgkin's lymphoma and had found that it met the criteria. But when it came to breast cancer, there were problems with the data. The data were insufficient. We had problems comparing the groups. We found that while there was a higher survival, that it was not statistically significant. It was increased morbidity and mortality.

What was most needed what was not being conducted in the United States were multicenter randomized controlled clinical trials even though one in nine women in America have breast cancer.

Now, it became very controversial. It has been played out in the media. We had several lawsuits but what was needed was someone to step forward and say we will initiate this data collection and we will fund it and the Blue Cross/Blue Shield Association took the lead. The only way you are going to resolve the controversy is to take it out of the courtroom and put it where it belongs which is back in the clinical trial setting.

We worked with the National Cancer Institute to initiate these trials. We considered a cooperative effort with the NCI and with major research institutions. Today we are funding four clinical trials, two for stage two and three breast cancer and two for stage four breast cancer.

They have been successful. We have 17 plans and our Federal employee programs who support this, 40 percent of the subscribers in Blue Cross and Blue Shield have access to these trials.

Furthermore, two of the trials are ahead of schedule we think because of the financing. The accruals are better than projected. We think if you didn't have these trials, you would not have these trials either started or completed.

Finally, we would like to make some recommendations about how you can improve the quality and quantity of the clinical research. First of all, as a payer we have enormous demands on us to do similar kinds of things. What we don't have, you have heard all the entities today. The FDA, the agency, the Veterans Administration, the National Institutes of Health, some entity has to step forward and prioritize a national agenda for research.

Second, they have to say these are qualified studies.

Also, Mr. Chairman, we would like to support the recommendation you have made for incentives. We think you are right on target to talk about targeted incentives and voluntary incentives. But it has to be for all the parties involved in promoting clinical research.

That being the drug industry, the device industry, the payers, and the research institutions.

Thank you.

[Ms. Gleeson's statement may be found in the appendix.]

Chairman WYDEN. Very helpful. We will have some questions in a moment. Suffice it to say we are very interested in your thoughts about further incentives as well for payers, universities or others.

As I say, the real mark of not making something like that work is nobody will do it. In other words, they will just continue down their present paths. Further thoughts in that regard are helpful, and it seems to me that the association in regards to making available now information needs to be proprietary and deserves real credit and we will have some more questions in a moment. We appreciate it.

Ms. GLEESON. Thank you.

Chairman WYDEN. Ms. Quesnel, welcome.

TESTIMONY OF KIM QUESNEL, R.N., MANAGER, MEDICAL REVIEW AND UTILIZATION REVIEW AND TECHNOLOGY ASSESSMENT, BLUE CROSS/BLUE SHIELD OF MINNESOTA

Ms. QUESNEL. Thank you. I see the first words on my paper are good morning, but it is good afternoon. I appreciate the opportunity——

Chairman WYDEN. Fortunately, as has been in the case in some of these, it is not good evening.

Ms. QUESNEL. Well, I appreciate the opportunity to be here today and I thank you, Chairman, for inviting me from Minnesota to discuss technology assessment.

For the record, my name is Kim Quesnel. I am the manager of Medical Review and Technology Assessment from Blue Cross and Blue Shield of Minnesota. From this point on, I may refer to Blue Cross and Blue Shield of Minnesota as BCBSM.

The affordability of health care in the 1990's is the single overriding concern at Blue Cross and Blue Shield of Minnesota. We believe the ready acceptance of new technology by providers and the public and its diffusion are major contributors to the cost spiral in health care. New technologies are frequently implemented without addressing the value they add to the continuum of health care and their impact on outcome and cost.

Payers have developed skills in evaluating new as well as established and outdated medical technologies. BCBSM implemented a medical policy project in 1985 that has eliminated outdated technologies as eligible benefits and formally reviews new drugs, procedures, and devices. Five clearly stated criteria must be met before a new technology becomes an eligible benefit, which Susan did describe.

Good decisions can be made through the process I just described. However, the quality of the decision and the strength of the rationale depend on the availability of data from well-designed clinical trials, data that have been subjected to rigorous statistical analysis, and published in peer-reviewed journals. When data are limited or nonexistent, the reliability and validity of the outcome of a formal technology assessment can be legitimately challenged.

For several years, BCBSM worked closely with the trade association representing entrepreneurs and larger companies in the health care industry in guiding their research and development. We have encouraged the innovator to meet with us early on as they develop a product. Our goal is to keep communications open and to encourage and educate them on the necessity for good data demonstrating improved outcomes and cost-effectiveness.

We believe the payer must be a smart buyer. BCBSM has had a number of opportunities to work with local providers to help finance the collection of data while making promising new technology available to our members.

Examples of this are pilot programs we established with local physicians and hospitals on the laparoscopic cholecystectomy and laparoscopic hernia procedures several years ago. We also contracted with the Mayo Clinic and a local manufacturer to assist in gathering data on an implantable cardioverter defibrillator before it became FDA approved.

We believe participation in these studies on a limited basis is clearly in the best interests of patients, physicians, and the insured if the technology is superior to existing technologies, the health benefits are demonstrated, and financial risk is minimal.

In summary, the value of technology is highly subjective in the absence of data that establishes the impact on patient outcome and the cost-effectiveness of the technology compared to its alternatives.

Rigid and premature judgments about the value added of a new technology or a new application of an existing technology could easily have a negative impact on patient care, the viability of innovative small firms, and the loss of valuable products from the marketplace.

Financial incentives to those firms engaged in research and development may be desirable. Just how desirable would depend on the structure adopted to implement such a strategy. We believe that education of those involved in innovation through their trade organizations and the setting of standards for research design, data acquisition, and data reporting is reasonable and necessary.

Thank you for your attention this afternoon. This concludes my oral testimony.

Chairman WYDEN. Well, thank you both. It has been very helpful.

It seems to me that there is another interesting point in all this that needs to just be set out and I would be interested in your reaction. Blue Cross and Blue Shield, and you all have talked about some expensive trials, some trials that cost a lot per trial certainly in the public interests. It is in the interests of your subscribers and certainly in the interests of everyone, particularly given the changes in making available some information that used to be proprietary, but I think it would be fair to say that this would be in the long-term interest of Blue Cross as well and it would be in the long-term interests for our country to get other payers to do it because to the extent that you can get a handle on some of these research problems or problems discovered in this early research now, you don't get into a situation where 8 to 9 years down the road you

have this mega-crisis on your hands and you are playing catchup ball.

Is that fair to say, Ms. Gleeson?

Ms. GLEESON. Yes, I think that is absolutely fair. I think you have those mistakes that have been made in relation particularly to breast cancer. We probably spent 50 years performing radical mastectomies when they weren't indicated because we didn't have the comparative trials. When we did, we found out that we could have just as effective surgery without as much mutilation.

I think the worst thing that could have happened with a high dose chemotherapy and ABMT treatment was that it would have been allowed to be diffused without being tested, because all the women would have had it and we never would have known what really works. If it works, we ought to pay and pay promptly. But if it doesn't, we ought to take that money and invest it in something that will work.

Chairman WYDEN. That is too logical. The Federal Government isn't going to get into that business right away. But seriously, that is exactly what we are trying to do. I mean, that is what this is really all about, is to take this enormous technology dollar, this dollar that has got the opportunity to do so much good and do it in a way that also generates some savings as we try to, rein in the costs overall and build it around just what you are talking about.

Let me ask you one other question in terms of incentives particularly. You started moving down that kind of food chain a little bit, beyond the drug companies and the device companies. We would be very interested in the idea of incentives to get large payers to start doing more of what you are talking about.

What do you propose in that regard? I know that there is a process for formal Blue Cross/Blue Shield policy recommendations and all the rest. Don't feel you are bound to some kind of official position here, but I would be interested in just in what your thoughts might be of some ideas we could look at in terms of incentives that would be attractive to payers.

Ms. GLEESON. Mr. Chairman, I would be happy to share our thinking with you. At this time we don't have an official policy. I guess what I would like——

Chairman WYDEN. That is even better. Then you are not going to get in trouble with the Washington office.

Ms. GLEESON. Right. I guess what I would like to do is tell you a little bit about the environment we exist in, who wants coverage from us. One of the things you have to remember is that a lot of the costs you heard today about the costs of clinical trials, about the costs that the agency would have to underwrite is the cost of collecting data and analyzing data. In many cases that compared to the patient care cost, which is the cost that would—people would like to regulate to the insurers. That patient care cost can be very high.

In our ABMT trial, the cost to the National Cancer Institute was $3,000 to $4,000 per patient. The cost that we are contributing is 67,000 per patient, so it is not insignificant in several cases.

The people who would like us to pay the patient care costs, the National Cancer Institute would like us to pay all the patient care cost for all their controlled clinical trials. The drug industry would

like us to pay the patient care costs for all the drugs that are classified as for treatment, investigational new drugs, the treatment IND.

The device industry which you heard earlier would like us to participate in the patient care costs on a contingency basis to help them get the data so they can get approval. Then there are other proposals that say we should pay the patient care cost of any care review trial.

Well, we can't do all this. We just don't have the premium dollars. You can't insure 37 million uninsured Americans, pay for what is at least deemed to be acceptable medical practice, and fund this huge research agenda. Everyone has constraints. The National Health Institutes only approve 18 percent of the trials that are put before them. That is only for data collection and analysis.

So I think an important thing if we were to go forward, clearly breast cancer treatment is a major issue, but when we are confronted with what would be the next if we were to institutionalize our funding, we could really use help through some kind of a Federal research advisory board who could integrate the research needs and establish priorities for this country.

If you say what are the national priorities in health research for this country, there is no entity to go to. They could also speak to the study design.

Chairman WYDEN. Before we leave that, what you are almost calling for, it seems to me, is something we know something about in Oregon and that is with respect to research, the Federal Government instead of pretending to be able to do everything should designate some research priorities.

Ms. GLEESON. Yes, that is correct.

Chairman WYDEN. Then with respect to the additional assistance to get into study design and the like but the tough call—the tough call in this whole health debate and one of the things that I have expressed considerable concern about is that nobody wants to make any tough calls. Nobody wants to make any judgments you know about priorities. They are just going to pretend to be able to do it all and we want to make sure as we look at some of these other areas such as comparative clinical research that we don't pretend, like you say, to be able to snap our fingers and make it all happen. I am very receptive to this concept you have of trying to make some tough calls and get research priorities.

Ms. GLEESON. I think it is key. I think what you are seeing driven now in the research agenda in the clinical area, you have heard the discussion of the prior panels, if it has had a sponsor, we might have major clinical issues in the United States which the Government could issue the call for research in those areas, maybe there isn't a sponsor. The reason that we could step up to high dose chemotherapy with ABMT is there is not an unidentifiable sponsor.

Who is going to benefit if it is demonstrated to be effective? It has really a very diffuse sponsorship, so it needs someone to do that.

Chairman WYDEN. If anything, it might be attractive to a private sector participant because they would be participating in what amounts to almost a national challenge.

Ms. GLEESON. Correct.

Chairman WYDEN. The Federal Government would have set out an agenda for research priorities and a private sector participant would I think reflect incredibly on themselves.

Ms. GLEESON. A second issue I would like to bring up is if you wanted the payers to participate. Our recommendation is it not be a part of the coverage. Coverage implies it has gone through some kind of a review process like our technology evaluation that we find benefit and that if we find benefit and that is drug companies and the device companies have a right to include their research costs to make a profit, the hospitals can make a profit, but when you are talking about trying to make a contribution to clinical research and the benefit is unknown, there shouldn't be a discussion of profit.

We would like to see a separate financing mechanism like we established for the ABMT demonstration project. Basically it is not coverage. It is not a benefit. We made a contribution to the research institutions to help them defray the costs, patient care costs. We made a lump-sum contribution. We do not deal with claims and we wire transfer the money immediately.

What we have been able to do is to support these trials without it being costly. The average charge for ABMT is $120,000 to $150,000. The average contribution which we are making which the institutions have accepted to cover the cost for that patient and they will not bill the patient is $67,000. You can negotiate much better. So we would encourage that.

Finally, as payers, we need safeguards. We are not going to be able to pay or to support financially all the trials. We if we pay for a part of them and not all of them, in our litigious environment someone would like to sue us, so we would like some kind of legal safeguards.

Finally, I think the problem we are really grappling with is how are we going to fund it. While this trial was expensive, it was funded through nonpremium dollars. Our plans were able to come up with foundations, going back to employers, doing all kinds of things to come up with this money, but if we want to broaden this concept, it is hard to imagine it not coming out of premium dollars because that is really the only source for much of the insurance industry.

The problem is if we were to start broadening this concept in paying for it, we will be competitively disadvantaged in the marketplace because our premiums will be much higher. So I think we have to think of a way to give tax credit, we have to think of a way to reimburse the insurer, but there has to be a way to have a level playing field so we don't get disadvantaged on our own premiums.

Chairman WYDEN. Before we go on to tax credits, which of course involve, returning your tax dollars and that of everybody else in the room to everybody again and its impact on the deficit and the like, let me ask you both and I don't want to have you be unscathed here, Ms. Quesnel, what is the impact if under health reform all the payers, everybody, we don't have one or two people disadvantaged, are collecting and reporting certain minimal data on patient encounters with the health system? Talk about a patient's ailment, what treatment they received, what happened to them afterwards, what effect does that have on the payers.

Either of you, as Blue Cross looks at having gone it alone and by themselves and figuring out what this means competitively, how does this stack up if everybody has to do it?

Ms. GLEESON. I think there are different kinds of information you can collect that way, Mr. Chairman. You can collect trend information to check on the health status of a population to see if the health status is improving or not improving. When you get down to trying to find out the comparative efficacy of a technology, you can't generally get the data out of those kinds of studies. You have to have prospective, very detailed studies.

So we would support and it is not President's proposal that they collect data on health status, but the health status information won't answer the question on comparative technologies.

The President does have a proposal that pays the—that asks the payer to—it is a broad mandate that covers everything. I mean, I think we just have to be realistic and realize that you can't accomplish the goals. You can't pay for the uninsured, pay for general practice and the whole research agenda and I—the NIH can only fund 18 percent of its research. Every business goes through a priority setting process. I think that is one of the major contributions that could be made.

Chairman WYDEN. Ms. Quesnel, what are your thoughts on this, if everybody is collecting and reporting data?

Ms. QUESNEL. Well, obviously, it is helpful because it gives us more to look at, but, as Susan said, we need comparative data.

The other thing that is helpful in that sense, and Susan just alluded to it earlier, is that what has happened with the litigation environment and the positions that we are put in. So obviously, the more data, the more research that is being done, it is helpful for us to make better decisions.

Chairman WYDEN. One last question, maybe more appropriate for you, Ms. Gleeson. On the matter of the autologous bone marrow transplant and the chemotherapy for breast cancer, do you feel that your data is sufficient to conclude this at this time?

Ms. GLEESON. There are four studies, Mr. Chairman. Two for the earlier stages of the disease, stage two and three, and two trials for the metastatic or stage four. Early in 1994, we will have the first results from the stage two and three trials and those will be reported by the NCI. These are NCI designed and approved trials. They are done by the cooperative cancer groups.

We certainly have made an investment with the understanding that when these trials are concluded, that we will be able to differentiate the benefits between high-dose chemotherapy and ABMT from conventional treatment.

Ms. QUESNEL. Our plan in Minnesota is also one of the plans that do participate in the study and we have three institutions in our State that do participate, which has been very beneficial and educational for us.

Chairman WYDEN. We had some folks from Duke talking in a very upbeat fashion about this therapy recently. Are they involved in your study?

Ms. GLEESON. Yes. Dr. Bill Peters from Duke and his program is involved in this study. In fact, it was Dr. Peters' protocol that

was adopted to be used in the multicenter trial, stage two to stage three.

Chairman WYDEN. Well, you all have been very helpful and one of the things that I am really struck by is how exercised, big buyers—big payers like yourselves are about trying to get good comparative data now.

You would think in our country, particularly as you look at so many other segments of either governmental policy as it relates to the environment, as it relates to private sector with groups like the physicists getting out information through modern technologies that we would have a handle on health care technology. But clearly the fact that some of you are kind of staking out on your own, heading off into the wilderness to try to come up with some new models as payers is very constructive.

I am especially attracted to this idea, Ms. Gleeson, you have about trying to make an agenda of research priorities. I am convinced that when it comes to health care, I mean, we could literally pick all the funds in sight, whether it is in terms of national health reform or research and under any kind of approach, you still have to make some tough calls in terms of trying to allocate dollars in a thoughtful way.

So we would very much like your ideas as payers in terms of how we could incentivize further the proposal we have so as to make it attractive to people like yourselves. It is commendable that Blue Cross and the Blue Cross network is sort of going out and trying to do it on its own, but the fact of the matter is there are a lot of payers and a lot of programs in our country that aren't even in the position to do it even if they were convinced of the wisdom of it. So we have got to figure out a way to build this into health reform.

You all have been very patient for sitting through 4 hours or so of this nonstop debate which from time to time got a little bit arcane and I really appreciate all your involvement and we will be consulting with you all in the days ahead. Thank you.

The subcommittee is adjourned.

[Whereupon, at 1:04 p.m., the subcommittee was adjourned, subject to the call of the Chair.]

APPENDIX

Mr. Chairman, today's hearing about improving medical information so that doctors and patients can make more knowledgeable and efficient health care choices is important.

Witnesses here today will discuss how they feel the current system is lacking in providing incentives for industry to complete comparative studies between medical products. In preparing for this hearing, it has become crystal clear that--like health care reform in general-- the problems we are asked to discuss are highly complex. It appears that although members may be seeking the same end points, how they arrive at the prize will significantly differ.

I support efforts to expedite FDA review of drugs and devices. We need to help create an environment where federal regulators are partners and not adversaries in health care technology. While in Europe it may take only 25 government regulatory officials to approve a medical device, it can take more than 260 full-time officials at the Food and Drug Administration (FDA).

The health care device and drug industries ~~our~~ are two of the nations true success stories---where the U.S. clearly and unquestionably leads the world in finding life-saving products. Whatever this subcommittee or Congress decides to do on this issue or health

care reform, we must not compromise the ability of these entrepreneurs to compete and innovate.

I philosophically believe that increased competition is the key to bringing health care costs down. I discussed the issues of comparative studies and outcomes research within the device industry with doctors and hospital administrators in my district. They told me more should be done--but that under today's increasing cost pressures, they were making tough decisions and making them in the light of day. They said in Texas where there is no cap on medical liability, we make sure that we have sound information on the safety and effectiveness of drugs and devices. They also said when a salesman calls on them, if they do not trust or cannot verify clear treatment improvements or cost savings, they don't buy it.

Furthermore, I have major differences when it comes to who will be the arbiter of new technologies. I do not want the federal government becoming the referee, subjectively determining which device they feel is best for the health care treatment of my constituents. I have more faith in the health care professionals of West Texas than bureaucrats in Washington.

Finally, Mr. Chairman, because it appears that small businesses will be tasked with paying for much of the President's health care reform, and while we won't hear from them today, I will work with the Chairman so that in future hearings we have their input.

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COMPARATIVE DATA ON THE EFFECTIVENESS OF DRUGS AND DEVICES: A PRESSING NEED OF DOCTORS, PATIENTS, AND PAYORS

Testimony before the House Subcommittee on Regulation, Business Opportunities, and Technology
Washington, D. C.
October 21, 1993

presented by
Jerry Avorn, M.D.
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Mr. Chairman, and members of the Committee:

Thank you for inviting me here today. My name is Jerry Avorn; I am an internist, geriatrician, and health care researcher at Harvard Medical School and the Brigham and Women's Hospital in Boston. I am pleased to share with you some ideas on how we can make the nation's great resources of medications and devices better serve the needs of our patients, at a time of increased cost containment and calls for expanded access to health care. My comments today are based on the work of our research group at Harvard as well as the input of an Expert Panel on Medications and Aging which I had the privilege of assembling with a grant from the John A. Hartford Foundation of New York City. This group represented about a dozen experts drawn from medical schools, government, and industry. They were brought together to develop a plan for improving the use of medications among the nation's elderly. An expanded version of some of what I have to say can be found in the panel's final report, which I am making available to the Committee today. As in many aspects of medical care, the elderly represent the population for whom these issues are most pronounced, but the points I will be raising here also have applicability across the entire age span.

Allow me to deflate a myth that is believed in by many, perhaps most Americans. The myth is that when you go to visit your physician, he or she is armed with adequate information about the advantages and disadvantages of the various medications available to treat your particular problem, compared to one another. It's a very plausible myth. I, too, would like to believe that as I get ready to write a prescription, or when I teach medical students or interns and residents, I could turn to a solid base of research data to help answer the following real-world questions:

- Which of the many available arthritis drugs is the most effective for the commonest form of this disease, and which has the lowest risk of potentially fatal side effects?

- For a man with difficulty urinating and an enlarged prostate gland, who faces the options of prostate surgery, long term use of a medication, or simply "watchful waiting," what is the likelihood he will have relief of his symptoms, or complications, with each of the three alternative approaches?

- Drugs are available to treat high blood pressure at a cost to the patient of under $10 for a year of therapy, or over $1,000 for a year of therapy. How do these drugs compare in their side effects, and in their ability to prevent the long-term complications of high blood pressure such as stroke, which is after all the main reason we treat hypertension in the first place?

- How do answers to all these questions differ if the patient is 80 years old rather than 50 years old?

The information I need as a doctor to answer questions like these adequately is simply not there, and it is not there for any doctor in the country. The reason it is not there is that it is presently no one's responsibility to do the research needed to generate such information, or to make sure that it is available to the practicing physician when he or she makes recommendations to the patient. Let me be clear why this is the case. The Food and Drug Administration has the mandate to make certain that all drugs approved for use in the United States are safe and effective, and by and large it performs this task well. But it is *not* the legislated mission of FDA to compare drugs with one another to see which is better, or more cost-effective. In fact, the main requirement imposed by FDA is for a drug manufacturer to show that its drug is better than nothing, a placebo. FDA officials will be the first to point out to you that it is not their job to evaluate drugs beyond this point, and they seem to have no enthusiasm for taking on this new role.

Nor is it prudent public policy to expect drug manufacturers to come forward voluntarily and subject their products to tougher testing than is required of them. They do engage in some comparative evaluation if they feel that it will show their product in a good light, but that can leave a lot of important comparisons untested. Foremost among these are comparisons with time-tested old standby generic drugs, which very often are every bit as good as (and in some cases even better than) much more costly patented drugs. However, there is very little reason for companies to fund studies to evaluate these inexpensive drugs, on which no one is making huge profit margins any more.

So there are really two components to the myth about how much information is available to your doctor when he or she is writing a prescription. First is the myth that this kind of comparative information is in existence, which it often is not; second is the myth that it is the responsibility of some organization or industry or set of individuals to make sure that such data are in place. No one has such a responsibility.

This is not because such information would be impossible to generate. It would require large-scale clinical trials, observational studies of huge numbers of treated patients, and epidemiologic studies of populations. These can all be done. My colleagues and I at Harvard Medical School and the Brigham and Women's Hospital in Boston do this kind of research, and it is frankly much less difficult than building a superconductor supercollider or fixing the Hubble telescope. The problem is, there's not much interest in supporting such research. FDA has very little money available for university-based investigators, and as I mentioned it does not see its mandate as including this kind of work. The National Institutes of Health sees its role as supporting basic biological research, and often has a rather condescending attitude toward mundane studies comparing different ways of treating patients' common clinical problems. NIH does not see this as part of its core mission, and has not been eager to fund such research.

People have suggested the pharmaceutical industry might be a plausible source of support for this kind of drug research, since at present the research budget of the pharmaceutical industry surpasses the research budget of the entire National Institutes of

Health. NIH officials therefore assume that such studies ought to be supported by the pharmaceutical industry. However, it is naive to think that a company that has invested a nine-figure amount in developing a drug will be enthusiastic to subject it to a costly study comparing it head-to-head with an older product that may cost a tenth or a fiftieth of its price.

There is a small agency within the federal government that has been given the mandate to support this kind of research, the Agency for Health Care Policy and Research. However, that mandate is not matched by its pathetically small budget, which is one of the tiniest in the entire federal research system. In one recent grant review cycle, the agency was forced to deny funding to about 90% of the grant applications submitted to it, many of which were quite good, because it could afford to fund only about 10% of the research proposals it received.

Are there people out there who could perform such research? Certainly. Our universities and teaching centers are full of bright young physician-investigators who have seen the irony of this information gap in their own training and daily practice, and who have been trained to perform such studies. There are also dozens of skilled contract research organizations in the country who are quite adept at running large numbers of patients through clinical trials, but whose only clients thus far have been drug companies seeking FDA approval of new products.

Given the paralyzing budget deficit which is our legacy from previous administrations, this is not a good year to propose another way for the federal government to spend money. This is paradoxical, since it is a year in which we are discussing having the federal government underwrite several billion dollars of medication costs for the elderly even now, the federal and state treasuries are spending tens of billions of dollars per year to pay for drug coverage through the Medicaid program. If a fraction of a percent of the public monies spent on medications were made available for this kind of comparative research, the investment would be repaid almost immediately in terms of better information to help doctors to provide the most accurate, cost-effective care possible for our patients.

There is one source of support that has not been devastated by twelve years of fiscal irresponsibility, and that is the private sector. Employers, insurance companies, and health maintenance organizations collectively will pick up a very large share of the nation's 70 or 80 billion dollar drug bill in the coming years. It is very much in their immediate financial interest to be able to know which medications work better than others, which incur the fewest side effects, which have the best long-term profile of effectiveness, and which are the best buys economically. In the absence of such data, these heavy hitters are spending billions of dollars per year more on medication than they need to, as well as on procedures and devices, which also have not been subjected to rigorous comparative scrutiny. What is needed here is a catalyst, Mr. Chairman, and you and this committee may be ideally suited to provide that kind of leadership. Payors, both public and private, need this information, practicing physicians want it, and, most important of all, the patients of this country deserve

it. Huge sums of money are already being spent on health care, and this is not a call for us to spend more. Rather, it is a demand that we as a nation do what is done by every competent company involved in technology in any way: set aside a small fraction of annual revenues to learn how we can do the job better.

Without this kind of leadership, several unappealing scenarios are grimly predictable. The first is that a brainless spreadsheet mentality will come to dominate this problem, and we have already begun to see that happening. What I mean here is the view that what is cheap is always what is most cost-effective. We need to be more sophisticated than that. Some expensive drugs are among the very most cost-effective interventions in all of medicine, despite the "sticker shock" which their price might convey. This may be because they are more effective in the long run in preventing use of those really costly components of the health care system: hospitalization, nursing home care, or surgery. We need sophisticated clinical and economic analyses to evaluate the entire cascade of events flowing from the use of medications; this will frequently lead to conclusions quite different from the "cheapest is best" approach. This involves pulling together pharmacologists, economists, epidemiologists, physicians, and people from several other disciplines. It can be done, and we have made some steps in this direction in my research unit at Harvard. But we are only one small group of investigators, and the nation needs such information on a much larger scale.

In closing, let me make one final observation on how this relates to the current very promising movement we are seeing toward reform of the nation's health care system. One critical "missing link" seems to be absent in virtually all of the plans that have been put forward for delivering affordable, excellent medical care to all citizens. It may be the result of the heavy influence of economists and other "policy wonks" in shaping health policy on both sides of the aisle, often to the exclusion of clinicians. Whatever the cause, the nation is getting the message that if we can just restructure the financial incentives of health care providers, whether they are physicians, nurses, or the larger organizations which will employ us, this will somehow make cost containment happen, which will in turn make it possible to have greater access to care. This brings us back to the myths with which I began my testimony. You could put a gun to the head of the most competent and committed physicians in this country, Mr. Chairman, and tell them to practice more appropriate, cost-effective medicine, but if they do not have the informational infrastructure available to them to know what in the world *is* the most cost-effective approach for a given problem, they will not be able to do so. We are spending enough money on health care. We simply need to spend it smarter, by identifying which drugs, procedures, and devices work best for which patients, and which do not. As a nation, we seem to have forgotten in the last decade that a great deal of good can come from everybody chipping in a small amount to achieve important goals that will benefit society as a whole. There are hundreds of thousands of physicians and other health care professionals in this country who would like nothing more than to do the very best job available for our patients. If we want to make the goals of health care reform a reality, we had better get started in helping to generate the information that is needed to accomplish this goal.

Thank you.

REPORT OF THE EXPERT PANEL ON MEDICATIONS AND AGING

Prepared for the John A. Hartford Foundation of New York City

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INTRODUCTION

The Expert Panel on Medications and Aging was convened by the John A. Hartford Foundation as a national panel of authorities in the disciplines in geriatrics, gerontology, epidemiology, health services research, public policy, and pharmacology. Its mandate was to provide a consensus report critically examining the need for further work to improve the effective use of medications by the elderly. The project was supported by a grant from the Hartford Foundation to the Program for the Analysis of Clinical Strategies, Gerontology Division, Brigham and Women's Hospital and Harvard Medical School (Jerry Avorn, M.D., Project Director). The following represents a synthesis of the work of that project. The positions and opinions expressed below are extracted from reviews of the relevant clinical and policy research, over two hundred pages of transcript of the expert panel's two meetings in Boston, ancillary meetings held with other authorities in these fields who are not members of the expert panel, a structured 38-item survey instrument administered to panel members and reviewed at the group's last meeting, as well as supplementary statements by panel members. While supported by the John A. Hartford Foundation, these recommendations are designed to inform all participants concerned with medication use by the aging, to guide future activities over the coming years on the part of health care providers, regulators, and funders, as well as researchers, clinicians and other caregivers, and patients themselves.

A NOTE ON METHODOLOGY

The recommendations which follow were developed in a multi-step process described briefly below.

The project director (Dr. Avorn) consulted widely with representatives of numerous groups related to medication use in the elderly from several fields (geriatrics, health policy, pharmacology, epidemiology, regulatory affairs, consumers, etc.) as well as with Hartford Foundation staff (Dr. Regenstreif and Ms. Robbins). A potential list of candidates for membership on the expert panel was developed and circulated. After additional consultation, a final list was formulated, and its members contacted about participating in the work of the expert panel. Nearly all those contacted agreed to participate. The charge to the group was explained, and the group met initially in Boston November 4 and 5, 1992. The first part of this meeting was an open-ended "brainstorming" session designed to bring forward a wide array of all possible issues related to improving medication use by the nation's elderly. In the afternoon of the second day of the meeting, these were condensed down to a series of programs and potential areas of intervention. The meeting was recorded and transcribed verbatim.

Following the Boston meeting, an invitation was sent out to an additional group of people with expertise in areas related to the project, who came together during the annual meetings of the American Geriatrics Society and Gerontological Society of America, held in Washington, D.C. in November 1992. The goals of the project were presented to this group, as well as an overview of the deliberations held in Boston the preceding month. This group provided reactions to and perspective on the product of the Boston meetings, as well as adding some additional areas for consideration.

During early 1993, specific areas were pursued and developed further with individual members of the expert panel. The transcript of the preceding meetings was reviewed, and from it were extracted a series of questions concerning the current status of the field as well as 25 specific areas identified previously as potentially ripe for future activity. These were divided into four major categories:

- Drug testing, development, and labeling
- Improving prescribing and utilization
- Measuring the effects of marketed drugs
- Economic issues

Summary statements concerning each potential activity were developed, and members of the expert panel asked to assign each a score between 0 and 5 indicating its priority for further activity in efforts to improve the utilization of medications by the elderly (5 = highest priority, 0 = lowest priority). This material was circulated to the group prior to the second Boston meeting, in enough time for project staff to tabulate the scores and return a summary document to the members for their consideration prior to the meeting. The expert panel re-convened at Harvard Medical School July 6 and 7, 1993 to review these issues as well as additional materials. The recommendations which appear below are based directly on the scores provided by expert panel members, as well as on the 122-page transcript of the second Boston meeting. As a final check, all members of the expert panel will review this document and modify it as needed to reflect the group's consensus.

OVERVIEW OF CURRENT STATUS OF THE FIELD

There was strong consensus concerning two central attributes of medication use by the elderly in the context of the overall health care enterprise. For each of the areas listed below, panel members indicated that medications and aging had high inherent importance, but that the attention received for each item was very low. The data are presented in the table below, in which a ranking of 0 indicated minimal to no importance (or attention received), with 5 being the maximum score in each category.

Table 1: Medication use by the elderly: importance vs. attention

INHERENT IMPORTANCE	ASPECT OF HEALTH CARE SYSTEM	ATTENTION RECEIVED
4.3	impact on the health of elderly patients	1.7
3.9	pre-degree professional training of physicians, nurses, and pharmacists	1.2
3.9	continuing professional education	1.4
4.0	health policy discussions and planning	1.6
4.3	impact on quality of life of older Americans	1.2
4.3	role in iatrogenic complications in the elderly	1.9

The group then considered the current level of activity in this area being conducted by seven key organizations with direct relevance to this field. A score of 0 was assigned for minimal or no activity, with a maximum score of 5 for very effective activity in this area. In general, with the exception of the Hartford Foundation, respondents found little or no evidence for very effective activity in this field by the governmental, philanthropic, or corporate groups discussed. (The Hartford score was lowered somewhat by the observation

by some respondents that the question referred to "present level of activity," reducing the Hartford score on the grounds that no new initiatives in this area were currently being undertaken.) Because panel members represented a wide cross section of physicians, health care researchers, and federal officials, all of whom are quite familiar with the activity of all groups in this domain, the overview presented below is very likely to be an accurate depiction of the intensity of programs currently in place.

Table 2: Present level of activity concerning medication use in the elderly

ORGANIZATION OR AGENCY	AVERAGE SCORE (0 to 5)
Governmental agencies:	
Food and Drug Administration	2.5
Agency for Health Care Policy and Research	2.8
National Institute on Aging	3.2
remainder of National Institutes of Health	1.9
Private sector:	
pharmaceutical industry	2.5
The John A. Hartford Foundation	3.8
other foundations	1.5

Panel members noted that throughout the National Institutes of Health in the last decade there has been only a single request for proposals issued on the topic of medications and aging: a small program on geriatric pharmacology issued on a one-time basis by the National Institute on Aging in 1989, which resulted in the funding of about ten modest-sized research projects. A one-time request for applications issued by the Agency for Health Care Policy and Research in 1992 dealt with the effectiveness of pharmaceutical therapy in general, but did not address medication use in the elderly specifically. Following that

program, it was widely believed that AHCPR would launch a follow-up grants program to focus on medication use in long-term care facilities, and a preparatory meeting was held on that topic in 1992. However, at a time of very constrained funding at AHCPR, this program has not yet materialized. Possibilities are also severely constrained for investigator-initiated projects within AHCPR: in one recent funding cycle, the Medical Treatment Effectiveness Program of AHCPR was funding proposals at under the 10th-percentile level (i.e., available funds were so limited that over 90% of submitted applications could not be supported).

Another important governmental agency concerned with medications and aging is the Department of Veterans Affairs, which provides nearly a billion dollars annually in drug benefits to a patient population which is increasingly elderly. The VA has acknowledged the growing importance of geriatric pharmaco-therapy to its mission, and may be an increasingly active participant in this arena in the coming years.

Researchers concerned with utilization and clinical effects of medications in general have found in recent years that apart from a few large multi-center clinical trials, the National Institutes of Health prefers to focus its funding activities on the molecular basis of disease, viewing "applied" research as less central to its mission of advancing biomedical knowledge. Immediately before her departure as director of the NIH, Dr. Bernadine Healy ended the search for a new director of the National Institute on Aging by naming a basic scientist with limited experience in gerontology and none in geriatrics. It is not yet clear what effect this decision will have on the funding priorities of that Institute.

In the private sector, nearly all research funded by the pharmaceutical industry is understandably driven by the need to discover or promote specific products of a given company. Considerable funds and effort have been devoted by manufacturers to the basic

and clinical research necessary to discover and market specific drugs related to problems of the elderly, such as Alzheimer's disease and Parkinson's disease. However, support available from industry sources drops off sharply for the study of adverse effects of drugs in the elderly. Further, if a proposed research project or intervention is unlikely to improve the marketability of a currently patented drug, its chances of being funded are sharply reduced. One exception noted was Merck & Company, which has in the past year made a strong commitment to fund curriculum and patient education efforts in the general area of geriatrics. Ironically, because of the company's desire to not tie this philanthropic effort to its own products, the program does not emphasize medication use. In addition, the recent financial difficulties of the pharmaceutical industry have resulted in a diminution of the scale of this effort from that which was originally planned.

Concerning philanthropies, apart from the Hartford Foundation no other foundation active in health care issues (such as the Robert Wood Johnson Foundation, the Commonwealth Fund, or the Henry J. Kaiser Family Foundation) has targeted medication use in general or in the elderly in particular as an area for support. To our knowledge, none plans to move in this direction.

In summary, in assessing the present situation panel members felt that practice and research issues relating to medication use by the elderly are of central importance to the American health care system, yet receive disproportionately small attention in the training of health care professionals, as well as in the funding priorities of most public and private organizations nationally. The group then went on to review potential future areas of activity and evaluate each for its potential importance in improving the use of medications by the elderly.

DRUG TESTING, DEVELOPMENT, AND LABELING

Priority area one: Define gaps in the science base describing differential drug effects in the elderly.

Most panel members agreed with the "conventional wisdom" that the elderly are more susceptible to adverse drug effects than are the young, and may respond differently in terms of drug efficacy as well. However, it was noted that there is a real dearth of solid pharmacological and epidemiologic data bearing on these issues. This results in part from a perverse circularity: the very old (particularly the frail elderly) are still not well represented in pre-marketing studies of drugs, so that inadequate amounts of data are generated about such populations in such clinical trials. The panel was told that there is still skepticism at FDA concerning the magnitude and importance of differences in drug efficacy or toxicity that result from chronological age alone; this skepticism is based in large part on the absence of clear data demonstrating such age-related changes. In 1989 FDA issued a discussion paper designed to focus attention on this area (circulated to panel), but this has not yet been enacted into formal guidelines. FDA and the pharmaceutical industry representatives on the panel felt that ever-increasing numbers of older patients are being included in pre-marketing studies of drugs. However, data presented at the panel's first meeting appeared to indicate that often this represents patients in their late 60s, and in generally good health. The relevance of findings on such subjects to patients in their late 80s, or to those who have multiple co-existing medical problems, may be quite limited.

Proposed action steps:

- Commission a small series of projects followed by a consensus conference to better define the pharmacologic basis of age-related differences in pharmacokinetics, pharmacodynamics, efficacy, and adverse effects. This would be very useful in distinguishing those aspects of "conventional wisdom" which have clear clinical and policy relevance from those which are plausible but unfounded.

- Generate more precise information on the actual rate of inclusion of patients in all older age groups (not simply those "over 65") in new drug applications brought before the FDA in the last decade. Particular attention should be paid to the rate of inclusion of patients over age 75 or 80, as well as patients with typical co-existing morbidity and concurrent drug therapies.

- Based on the above, prepare updated guidelines for inclusion of elderly subjects into pre-marketing drug trials.

Priority area two: Develop strategies to enhance the recruitment of appropriate elderly subjects into drug trials

Because of the historical lack of prominence of elderly subjects in drug trials, investigators and representatives of the pharmaceutical industry on the panel indicated that enrolling adequate numbers of older patients in new drug testing is difficult because of the lack of experience with inclusion of such patients. Thus, even when there is willingness to recruit older subjects, they are often underrepresented because of the perceived difficulty in

their recruitment, and its attendant higher cost per subject. A workshop was conducted on this topic in September 1992 (proceedings being distributed to panel members) that made a good start in exploring some of these issues.

Proposed action steps:

- Convene a working group or conference of representatives of the clinical research departments of pharmaceutical manufacturers, geriatricians, biostatisticians, and regulators to address the following issues:
  - Determine the most cost-effective means of identifying, recruiting, and retaining elderly subjects for phase III clinical drug trials;
  - Define the statistical issues associated with analyzing data on subjects whose life expectancy may be shorter, and confounding characteristics more complex than younger subjects;
  - Develop quantitative and regulatory approaches to address these issues, to minimize the prejudicial effect of having more complex elderly patients enrolled in clinical trials;
  - Support the development of one or more consortia of elderly subject resources (to be drawn from academically affiliated long-term care facilities, the nursing home industry, or university based geriatric practices) to work with pharmaceutical manufacturers as resources for inclusion of more typical elderly patients into drug trials;

- Identify current barriers to include enrolling adequate numbers of typical elderly patients, and propose methods to overcome them.

Priority area three: Better identification of geriatric-relevant outcomes for drug development

Frequently, trials of new drugs will focus on careful measurement of a target therapeutic outcome (e.g., blood pressure), but pay inadequate attention to other outcomes which may be of particular relevance to the elderly (e.g., effects on cognition, mood, or gait stability). This is particularly problematic for older patients in whom the adverse effects of a drug in other organ systems may be more prominent than its therapeutic effect.

Proposed action steps:

- Initiate a series of consensus-development activities (through conferences, literature reviews, and limited projects) to define geriatrically relevant outcomes which must be studied in pre-marketing trials of drugs in several common therapeutic categories. Prominent among these would be functional status measurements such as effects on mood, memory, attention, mobility, and "quality of life."

- Particular attention should be directed to defining age-related changes in the relationship between intermediary outcomes (e.g., blood pressure, serum lipids, or intraocular pressure) and actual clinical outcomes of concern in the elderly (e.g., stroke, cardiovascular disease, and visual loss due to glaucoma).

Even when reduction of such intermediary risk factors by drugs has resulted in improved clinical outcomes in younger subjects (e.g., reduction of elevated serum cholesterol with niacin or bile acid resin producing a reduction in cardiovascular disease), the efficacy of such therapy has often not been convincingly demonstrated in the elderly.

Priority area 4: Labeling of prescription medications

"Labeling" refers to the federally required specification of indications, instructions for use, efficacy, dosing, and adverse reactions that must be published for all prescription drugs. Despite the high proportion of drug utilization accounted for by the elderly, for many commonly used drugs the approved labeling does not adequately address this population. Paradoxically, the official instructions for use for many drugs common in geriatric practice often contain far more information on the use of a given drug in pregnant women, nursing mothers, and children, than for geriatric practice. A set of proposed regulations on geriatric-specific labeling was circulated by FDA in 1990 (copy sent to panel members) but has not yet been made into a regulatory requirement.

Proposed action steps:

- Mandate universal inclusion in drug labeling of specific considerations for prescribing an agent in older patients, if the drug is regularly used by older age groups. Initially, given the current inadequate state of knowledge in geriatric pharmacology, for many drugs this section would have to indicate, "Inadequate information is available concerning use of

this drug in patients over age 70." However, within five years such information could be required of manufacturers by FDA as a condition for continued registration of a drug.

IMPROVING PRESCRIBING AND UTILIZATION

Priority area one: Provide information resources for professional schools and continuing education in the area of geriatric pharmacology

Geriatrics is still a minimal or absent in the curricula of many schools of medicine, nursing, and pharmacy; education in drug therapy decisionmaking is likewise given limited treatment in most medical school curricula. As a result, geriatric pharmacology is vanishingly rare in the preparation of most medical students and other health professionals. While the battle for curriculum time is a major problem in this regard, in many institutions the rate-limiting step is the lack of availability of good teaching materials. This is particularly the case in continuing education programs, where clinicians in practice are faced daily with challenges related to the use of medications in the elderly, and could provide an eager audience for education on this topic.

Proposed action steps:

- Develop and actively disseminate targeted curricula in geriatric pharmacology for insertion into pre-degree programs in the education of doctors, nurses, and pharmacists.
- Create an ongoing source of geriatric drug information to support standard postgraduate programs as well as innovative educational outreach initiatives for clinicians in practice.

Priority area two: Improve the scientific and epidemiologic basis for geriatric drug utilization review (DUR)

Despite the proliferation of federally mandated and proprietary computer-driven drug utilization review programs, there is little rigorous evidence to demonstrate any impact of such programs on clinical outcomes or on health care costs. Where such evaluation has been attempted, results have been disappointing. In addition, the decision rules on which such programs are based are often proprietary and thus not available for scrutiny by researchers, clinicians, or the public. When such rules have been inspected, some algorithms have proven to be clinically implausible, particularly for the elderly. Nonetheless, initial computer screening of prescriptions for appropriateness and cost-effectiveness, followed up by review by a trained clinician, may hold considerable promise for improving the quality and economy of drug use in all age groups, particularly the old. Unfortunately, this technology has proliferated before careful groundwork has been laid in its development or critical evaluation.

Proposed action steps:

- Evaluate the adequacy of current widely used DUR programs and their impact in influencing drug therapy for the elderly;
- Develop DUR decision rules which are more geriatrically and epidemiologically appropriate than those currently in use;
- Evaluate computer-based feedback of information at the point of clinical decisionmaking to inform physicians of the appropriateness of their prescribing for the elderly. Such programs should be developed and rigorously evaluated for use in hospital, community, and long-term care settings.

Priority area three: Critically evaluate the impact (both positive and negative) of regulatory and reimbursement policies aimed at medication use and the elderly.

Recent years have seen several initiatives designed to influence drug use in the elderly, ranging from the OBRA 1987 legislation concerning antipsychotic drug use in nursing homes, to various attempts at cost-containment implemented by state and private authorities. Frequently, such regulatory or economic interventions are implemented without any plan to evaluate their impact on drug use, clinical outcomes, or expenditures. Haphazard application on a large scale of previously untested interventions is commonplace for health policy interventions, yet would be considered criminal for specific pharmacologic interventions. Standards of efficacy and harm similar to those applied to new drug applications should be extended to the implementation of new programmatic interventions as well.

Proposed action steps:

- Document the effects (both positive and negative) of regulatory interventions designed to improve medication use in the elderly at the federal, state, and institutional level. Such evaluations must take into account not just the effect of the policy on medication utilization, but also its impact on use of other health care resources, patients' clinical outcomes, and total cost.

- Encourage the development and *prospective* application of such evaluations plans prior to widespread implementation of programs to influence prescribing, in order to identify which work, which do not, and which may be harmful to patients.

MEASURING THE EFFECTS OF MARKETED DRUGS

Priority area one: Conduct systematic post-marketing surveillance

Because of the low representation of the very old and frail elderly in pre-marketing studies of drugs, epidemiologic surveillance of adverse effects in large populations provides one of the most important means of detecting adverse effects not identified in pre-marketing testing. This would be the case even with ideal representation of the elderly prior to marketing, as some adverse effects will occur rarely or only in the face of unusual combinations of coexisting drugs or therapies, making them unlikely to be detected in drug testing prior to widespread use. Fortunately, a number of databases exist which can be used for such post-marketing surveillance. Prominent among these are claims databases based on the Medicaid programs of several states. Because Medicaid plays such a prominent role in coverage of nursing home care, these programs (and the databases describing utilization within them) are heavily enriched with frail elderly patients. Increasingly, as more older patients move into managed care settings, databases based on HMO care will also become efficient tools for pharmaco-epidemiology in this age group.

Proposed action step:

- Provide resources for ongoing, systematic epidemiologic surveillance of drug use in the elderly, and use this resource to:
  - generate regular reports on patterns of utilization (overuse, underuse, as well as potential mis-use)
  - develop new information on the frequency and causes of adverse drug effects in this age group.

Priority area two: Develop *comparative* information on the benefits and risks of commonly used drugs in the elderly, to guide drug choice decisions by clinicians and by health care organizations.

At present federal regulatory requirements demand that a new drug be shown to be superior to placebo, but there is no requirement for comparative testing of a new agent against commonly used similar drugs within its class. As a result, while all drugs approved are effective and relatively safe, the current system leaves the clinician with little systematic guidance concerning the relative advantage or disadvantage of, for example, a newly marketed non-steroidal anti-inflammatory drug compared with other drugs within this class. It is crucial that prescribers, patients, and payors be able to discriminate among similar drugs in terms of their risks, benefits, and price (see below), particularly in the elderly, who may be more vulnerable to suboptimal choices in all three domains. Current legislation does not require FDA to collect such information or require manufacturers to generate it prior to drug approval; indeed, some argue that the current legislation actually prevents FDA from requiring such data. However, a pluralistic system of payors such as currently exists, which will increase further under health care reform, presents opportunities for innovative means of generating such information. Even in the absence of new federal requirements for drug-to-drug comparisons, payors can require such information in evaluating drugs for formulary inclusion or determination of reimbursement level.

Proposed action steps:

- Identify drug classes commonly used by the elderly for which inadequate information exists concerning comparative efficacy, or side effects;

- Engage in "consciousness raising" among payors responsible for considerable elderly medication reimbursement (e.g., health maintenance organizations, insurance companies, the Veterans Administration, state Medicaid programs, Medicare in future years) to clarify the savings and quality of care improvements that would occur with availability of such comparative drug data.

- Help these groups form consortia to fund and/or conduct large-scale simplified trials to generate such information at reasonable cost in the context of normal clinical practice.

ECONOMIC ISSUES

Priority area one: Gather and disseminate data on cost-effectiveness of similar drugs commonly used in the elderly

The same arguments made above concerning comparative efficacy and toxicity apply equally well to the comparative study of cost-effectiveness of drugs. At a time of development of a new prescription drug benefit for the elderly covered through the federal budget, it is particularly appropriate that such large expenditures be made in the most cost-effective manner. However, the "most cost-effective" drug in a class may not be the same as "the cheapest"; all analyses of cost-effectiveness of medications must take into account the clinical and economic consequences of *all* outcomes associated with use (or non-use) of a given drug under study. This is particularly important in the elderly, in whom clinical outcomes which may not be immediately related to a drug's therapeutic indication (i.e., diminished or enhanced capacity for self-care) may have a major economic impact. Outlines for the proper conduct of cost effectiveness analyses of drugs have recently been published to guide such efforts (distributed to panel members).

Proposed action steps:

- Gather and disseminate available data on cost-effectiveness of similar drugs commonly used in the elderly, drawing on available literature;
- Calculate economic savings that could be realized from use of most cost-effective agents whenever possible, and make such information available to physicians and formulary committees;
- Work with payor consortia described above to integrate cost-effectiveness components into comparative drug analyses.

Priority area two: Link drug reimbursement to adequate data on a drug's effects in the elderly

It would be impractical at present to disallow reimbursement for all drugs with inadequate information about their use in the elderly, as this would remove many important agents from the available pharmacopoeia. However, in the coming years it will be possible to institute economic incentives for manufacturers to generate such data as described below.

Proposed action steps:

- Formulate policy options for private and federal payors to restrict payment for drugs which have inadequate data on effects in the elderly after a specific time post-approval; analyze impact of widespread of implementation of such policies;
- Consider incentives (patent life extension, more rapid pre-marketing approval, greater reimbursement through proposed Medicare drug benefit,) for products with well-documented profiles concerning geriatric effects.

Priority area three: Define the economic aspects of enhanced drug coverage for the elderly under health care reform

The expert panel engaged in its deliberations at a particularly exciting time in the history of American health policy. Major new entitlements are being proposed for prescription drug benefits for the elderly which are unprecedented in U.S. history. The changes which will be formulated in the coming year will have profound implications for the quality and consequences of medication use by the nation's elderly. It is crucial that such

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national debate be informed by comprehensive and accurate data concerning the economic and clinical implications of prescription drug coverage for the elderly. It will be important to learn from the lesson of the ill-fated Medicaid Catastrophic Coverage Act of 1988, which attempted to legislate a prescription drug benefit plan for the elderly with an inadequate data foundation, which contributed in part to its controversy and its eventual repeal.

Proposed action step:

- Develop economic models of expenditures for drugs by the elderly in different existing coverage plans, as well as projected coverage designs under health care reform. Use these models to provide recommendations to policy makers at the federal level as well as in the private sector.

* * *

In summary, this project made it possible to assemble a distinguished group of experts from widely varying disciplines, each of whom brought an important perspective to bear on the complex issue of medication use by the elderly. The group's deliberations occurred at a time of enormous progress in the development of new products of biological research, as well as unprecedented changes in the U.S. health care system. Underlying both is the inexorable increase in numbers of elderly (particularly the "oldest old") and their growing impact on the American health care system. As a result of this confluence of events, the conclusions and recommendations of the Expert Panel on Medications and Aging will be well situated to inform policy and practice at a pivotal time in the care of the elderly.

BEFORE THE SUBCOMMITTEE ON REGULATION, BUSINESS OPPORTUNITIES, AND TECHNOLOGY

Testimony of John P. Burke, M.D.

Hearing of October 21, 1993

My name is John P. Burke, and I am a physician. I am a Professor of Medicine at the University of Utah, and the Chief of Infectious Diseases at the LDS Hospital in Salt Lake City, Utah. I am also the immediate Past President of the Society for Hospital Epidemiology of America, an organization that fosters research to improve health care in hospitals.

For the last two decades, I have led a research team that has studied the effectiveness of drugs and medical devices. My experiences as an investigator have led me to the conclusion that our system for evaluating medical technology is badly flawed. Ideally, a synergy of government, industry, and independent clinical researchers would support the evaluation of drugs and devices. Unfortunately, at the moment, not only does industry often seem wary of large-scale clinical trials, but government agencies tend to unnecessarily delay clinical research. In the absence of medical facts, patients suffer needlessly and the nation's health care bill grows unnecessarily. Today I encourage legislation to streamline the process for clinical evaluation of drugs and medical devices.

I have encountered many of the problems that now plague our system. I offer two valuable lessons. First, that the fundamental component for evaluating medical technology is the large-scale clinical study, and second, that subjects in these studies must be typical patients. Regrettably, for the moment, it seems that we know the cost of everything and the value of nothing. For example, because manufacturers are so acutely aware of the high costs of developing a new product, they often bring it to market without proving its value. With so much at stake, manufacturers dare not expose a new product to a large-scale clinical trial for fear of discouraging results. Instead, manufacturers contract for small studies, in carefully chosen populations, that promise favorable conclusions. Such research may be less than independent and impartial since the manufacturer has the motivation, if not the ability, to suppress contradictory results. Furthermore, manufacturers often begin promoting a product even before its testing, however scanty, is complete. Thus advertising claims may amount to nothing more than wishful thinking. The net result is that new drugs and devices arrive for patient use before their efficacy and cost-effectiveness have been established. It is an unhealthy and dangerous situation.

My colleagues and I recently conducted one of many studies that illustrates these problems. We studied a silver-coated urinary catheter. Ordinary catheters are made of latex rubber, and are prone to causing infection. Manufacturers hoped that by coating the surface of the catheter with a disinfectant, such as silver, the risk of infection might be reduced. This innovation addressed a serious medical problem. Urinary catheterization is the leading cause of hospital-acquired urinary infection, as well as the most common source of fatal blood stream infections. And the costs from these side-effects may add as much as $2 billion to our health care bill every year.

The silver-catheter arrived in the hands of doctors after a single clinical trial. It was small and poorly designed. This study tracked a mere 74 patients who were not representative of the general patient population. Worse, the trial design failed to control for the variable being tested. Additional disinfectants were added to the catheter system, making it impossible to credit the silver coating with reducing the rate of infection. Yet it was this flawed study that was used to convince hospitals, doctors, and patients that the silver-coated catheter was worth its higher price tag.

Unfortunately, the advertising pitch was more effective than the product. Soon after its introduction, when we began our study, the silver-coated catheter had captured 20% of the market in our area. We then tracked 2,500 patients in a large-scale clinical trial. Our patient sample was not only statistically valid but representative of the patient population. Our results contradicted the small pre-marketing study. We found that the silver-coated catheter offered no benefit to patients. Even worse, male patients actually suffered a significantly higher rate of infection. Thus, rather than lowering the rate of infection and cutting overall costs, the silver-coated catheter hurt patients and bloated their--and our--bills. Clearly, then, this device is dangerous to both your health and our health care system. It is unsafe at any price.

Soon after we reported our results, the silver catheter was withdrawn from the market and its rights sold to another manufacturer that no doubt plans to reintroduce it with some slight modifications. Let us hope that any new design is proven effective in large-scale clinical trials before it is widely used.

We conducted our research with our hospital's sophisticated computer database for medical records. We have used this system to not only monitor but, more importantly, to improve clinical practice. For example, we sought to prevent adverse drug reactions in patients, a problem that afflicts 3% of our hospital's patients, adding about $1.7 million to our annual costs. We began this project by collecting data on the incidence of adverse reactions. We quickly realized the shortcomings of information about drugs collected during licensure testing. Most drug trials for licensure understandably include patients receiving only the experimental therapy. But such testing is only a first step. Drugs must also be tested under real clinical conditions, when they are often used in tandem with others. Our findings confirmed the need for such studies. We discovered, for instance, in the case of one antibiotic, known to cause convulsions in some patients, that the seizure rate was, in actual use, more than twice that predicted by its manufacturer. Our research suggests that this was not an isolated case. We must therefore be vigilant. The surveillance of drugs and medical devices must continue after they reach the market and the public.

We also found that our computer system could frequently identify potential problems and then warn the attending physician. We were thus able to dramatically reduce the rate of adverse drug reactions. In the case of the antibiotic mentioned before, we reduced the seizure rate from 5% to 0.2%, with annual savings to our hospital of $400,000. Indeed, our studies suggest that 30% of all adverse drug reactions are preventable.

We have also used our computer system to determine the efficacy and cost-effectiveness of drugs used in hospitals, a topic that has largely eluded scrutiny. This is unfortunate. At the LDS Hospital, by reviewing the cost outcomes of various antibiotics and then altering clinical practice, we achieved dramatic savings, despite the increased use of newer, more expensive antibiotics. In four years, in fact, the percentage of our pharmacy budget spent on antibiotics dropped from 42% to 14%. And, more importantly, we provided our patients with better care.

Our studies highlight the importance of large-scale clinical trials of both medical devices and drugs. The potential for cost savings and improved patient care is tremendous. As we have shown, health care costs can be cut by improving care. This should be a major focus of health care reform. Yet there now exists a funding gap for studies like ours. Neither the National Institutes of Health nor the Agency for Health Care Policy and Research accepts responsibility for funding these types of studies. In the past, our studies were supported by the National Institutes of Health. But now neither the NIH nor the AHCPR is targeting and supporting promising and necessary clinical research. And industry has not stepped in to fill the gap. I have been deeply disappointed that industry has not taken advantage of our computer-based surveillance system for evaluative research.

We must take steps to achieve synergy with industry, government agencies, and independent clinical researchers. Whatever the specific direction of reform, I believe that incentives for clinical research should be emphasized. Legislation should provide drug and device companies with inducements to fund large-scale clinical trials. For example, by lengthening the period of patent protection and streamlining the approval process, more and better drugs and devices might arrive on the market expeditiously. Preliminary FDA approval that would restrict use to certain sites where intensive surveillance would be conducted is an option that should be explored. Moreover, a "fast track" for FDA approval of drugs and devices would encourage both innovation and evaluation, bringing industry, independent researchers, and government together in the process.

BLUE CROSS AND BLUE SHIELD ASSOCIATION TESTIMONY

Before the

Subcommittee on Regulation, Business Opportunities, and Technology

October 21, 1993

I am Susan Gleeson, Executive Director of Medical and Quality Management for the Blue Cross and Blue Shield Association (BCBSA), an association of independent Blue Cross and Blue Shield Plans. I appreciate this opportunity to address the Subcommittee on the critical issue of the adequacy of currently available clinical data to support decision-making by practitioners and payers.

My testimony will touch on the following issues: the BCBSA's Technology Evaluation (TEC) program, the Association's breast cancer treatment demonstration program, the adequacy of current scientific information for technology assessment and limitations of existing clinical studies, the FDA review process for new drugs and biologicals, and, finally, the Association's recommendations for furthering meaningful clinical research.

The new role of health insurers in the era of health care reform will be to manage health care delivery systems in collaboration with practitioners to assure that members receive efficacious and appropriate medical care. Good data on the relative efficacy and cost benefit of technologies are the building blocks of rational decision-making. Such information is essential if the health care reform promises of universal access, cost control, and enhanced quality are to be realized.

I will begin by providing some brief background information on the Blue Cross and Blue Shield Association's technology assessment function. The BCBSA is the national coordinating agency for the 69 independent locally governed Blue Cross and Blue Shield (BCBS) Plans. The BCBSA serves as the cohesive force that brings these autonomous, non-profit Plans together into a national system. As a system,

we are the nation's largest and oldest provider of health care coverage, currently covering 67 million members or more than one in four Americans. Our Plans operate 92 health maintenance organizations (HMOs) and 56 preferred provider organizations (PPOs) nationwide.

The BCBSA provides many support services to Blue Cross and Blue Shield Plans. Technology assessment through the Association's Technology Evaluation "the TEC" Program is one of these services.

The TEC Program is one of the nation's leading technology evaluating entities, having conducted more than 200 assessments since its creation in 1984. The TEC Program examines and synthesizes the existing scientific evidence to determine the safety and efficacy of new medical technologies. The assessments developed by the TEC Program are scientific opinions meant to provide information to those who deliver and manage medical care.

The TEC Program uses five criteria to determine whether the technology in question improves health outcomes such as length of life, ability to function, or quality of life. Cost is not a consideration in technology evaluation. The five TEC criteria are:

1. The technology must have final approval from the appropriate government regulatory bodies.

2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.

3. The technology must improve the net health outcome.

4. The technology must be as beneficial as any established alternatives.

5. The improvement must be attainable outside the investigational settings.

The TEC evaluations are made available to all Blue Cross and Blue Shield Plans. Beginning in 1994, these TEC assessments will be made available to other interested parties. Many BCBS Plans will consider only technologies that meet all five criteria to be eligible for coverage. Such Plans find technologies that do not meet all the criteria to be investigational.

THE BLUE CROSS AND BLUE SHIELD SYSTEM'S
DEMONSTRATION PROJECT ON BREAST CANCER TREATMENT

A major issue for many insurers is the demand for coverage of a technology before there is data demonstrating its efficacy. One treatment that has been the source of much controversy is high dose chemotherapy with autologous bone marrow transplant support (HDC/ABMT) for breast cancer and other solid tumors.

Clinical studies of HDC/ABMT conducted thus far have not established that this treatment is as safe and effective as conventional chemotherapy in the treatment of advanced and early but high risk breast cancer. Many BCBS Plans exclude coverage for the treatment because they consider it to be investigational.

HDC/ABMT for breast cancer has been evaluated twice by the Association's Medical Advisory Panel since 1988, most recently in 1991 by David Eddy, M.D., Ph.D.

HDC/ABMT for breast cancer does not meet the five TEC criteria. There has been an absence of well-controlled trials, existing clinical series are poorly matched, and small differences in survival demonstrated between HDC/ABMT and conventional chemotherapy for breast cancer to date have not been statistically significant. Furthermore, treatment-related mortality and morbidity from HDC/ABMT exceed that from conventional chemotherapy. A fuller discussion of the deficiencies in data available from clinical trials is provided in the next section of this testimony.

Despite the lack of conclusive evidence that HDC/ABMT is as good as, worse, or better than conventional chemotherapy, coverage denials by BCBS Plans and other payers have generated unprecedented media interest and litigation. Some researchers advocate the treatment and women have sued, convinced that this treatment is their last hope. Some subscribers want access to this service regardless of the lack of scientific evidence supporting efficacy. Unfortunately, as a recent editorial in the Journal of the National Cancer Institute stated, some members of the oncology community "have raised the public's expectation far above what is supported by the published data. We have no evidence as of yet that any patient will be cured by this therapy who would not have been cured by more conventional treatment" (Henderson, 1991).

The Demonstration Project on Breast Cancer Treatment is an innovative effort to help resolve the clinical controversy surrounding the efficacy of HDC/ABMT for

breast cancer. The Demonstration Project is an attempt to return the debate to the appropriate forum of clinical research and away from the courtroom and television. Only well-designed research can answer the question "does HDC/ABMT work for breast cancer?"

The purpose of the Demonstration Project is to support randomized controlled clinical trials comparing the efficacy of HDC/ABMT with that of conventional chemotherapy in the treatment of advanced breast cancer and early breast cancer with a poor prognosis. The clinical trials are being sponsored by the National Cancer Institute (NCI), the Clinical Trials Cooperative Groups, and the Philadelphia Bone Marrow Transplant Group. It is hoped that increased financial support for this costly investigational treatment will speed accruals to the trials while providing our subscribers with access to this treatment. The Demonstration Project is supporting two multicenter randomized trials for women with Stage II/III breast cancer and 10 or more positive nodes (designated CALGB 9082 and INT 0121 by the NCI) and two multicenter randomized trials for women with Stage IV metastatic disease (designated INT 0127 and the Philadelphia Protocol, PBT-1).

The Demonstration Project provides financial support, on behalf of BCBS subscribers, to institutions that are participating in the trials and have entered into contracts with the BCBSA. The all-inclusive financial support payments are separate and distinct from coverage. They constitute support for clinical research and not benefit payments. The financial support payments defray a significant portion of the patient care costs of HDC/ABMT, including inpatient, physician, and ancillary services. Participating institutions are

expected to share in the costs of treatment as well.

Currently 17 Plans and the Federal Employee Program, accounting for 40 percent of our membership, are participating in the Demonstration Project. To date, 43 hospitals are participating and eligible hospitals are welcome to enter into contracts at any time. Several of the supported trials are accruing very well and we believe our support contributes to the rapid accrual.

BCBS Plans and the Office of Personnel Management for the Federal Employee Health Benefit Plans have been willing to invest resources in the Demonstration Project to obtain the clinical data necessary for determining the efficacy of this toxic and costly treatment. In the absence of such financial support, the trials might not be conducted or completed. These well-designed, large, randomized multicenter trials will provide the data essential for assessing this technology. Prior studies have been inadequate. During this period when efficacy is being evaluated, the Demonstration Project provides access to the treatment through trials for eligible women who are desperate to try any promising therapy.

ADEQUACY OF SCIENTIFIC INFORMATION FOR TECHNOLOGY ASSESSMENT

NEW DRUGS AND DEVICES

As my prior discussion of the TEC criteria and the Demonstration Project indicated, assessment of new technologies for clinical and management decision-making relies on scientific evidence that permits conclusions and comparisons to alternative therapies. Although a great deal of clinical research is conducted internationally and thousands of papers are published each year, many studies do

not provide clear evidence that can be used for technology assessment and selection of a preferred treatment option. Many studies no not follow proper scientific methodology and the investment in research dollars and time are wasted.

A recent TEC evaluation illustrates this point. The BCBSA evaluated Positron Emission Tomography for the central nervous system diseases in 1992. An initial review of the published literature for this evaluation identified over 600 clinical studies from 1980 through 1991 for 70 clinical indications. The studies were pared down to include only those that met minimum standards. Studies included were those that reported a clinical series, not necessarily trials, with at least six patients each and that were performed at a minimum of two independent centers. Only 33 studies (6%) survived this screening process and could be used for assessment of the technology.

I will summarize the major shortcomings of existing clinical studies:

- Lack of attention to basic clinical study design, including failure to define a hypothesis and design of the study to answer the scientific question
- Poorly chosen or absent control groups
- Overly small trials with too few patients to reach a scientifically valid conclusion
- Lack of clearly defined patient selection criteria
- Lack of clearly defined, objective outcome measures, starting points, and endpoints

- Insufficient use of randomized controlled groups and blinded evaluation of results even when no other study design can provide interpretable results, and
- Lack of patient follow-up consistent with the natural history of the diseases in question. For example, if disease recurrence is not normally expected for at least one year, follow-up periods of only several months are inadequate.

Thousands of clinical studies are published yearly. Many are poorly designed and cannot be interpreted. Payers and clinicians are unable to analyze and synthesize this avalanche of clinical literature, much of which does not merit analysis due to faulty design and execution.

FDA REVIEW

The FDA review process for new drugs and biologicals is very rigorous. The FDA is required to approve New Drug Applications (NDAs) only when the agency determines that the new drug meets statutory requirements for safety and effectiveness. The clinical investigations underlying claims of effectiveness must be adequate and well-controlled clinical trials. Expedited approval of drugs for life-threatening conditions continues to require well-designed controlled clinical trials. The BCBSA considers new drug approvals to fully comply with the TEC criteria for approved indications. Non-approved indications (off-label uses) may comply with the TEC criteria when evidence of efficacy for the off-label use appears in the clinical literature.

The FDA review process for devices is, unfortunately, not adequate for clinical and management decision-making. The FDA may review new devices through either the 510(k) review process to determine substantial equivalency with existing devices or through review of a Premarket Approval application. If a device is similar to other currently marketed devices in terms of its intended uses and technological characteristics, the FDA will determine that the device is substantially equivalent to those other devices. The FDA will "clear", rather than "approve" such devices for marketing without reviewing evidence of safety or effectiveness. The Premarket Approval process is the method used by the FDA to review and approve devices based on scientific evidence of safety and effectiveness. Only Class III devices not substantially equivalent to currently marketed devices are required to go through the Premarket Approval process. As a result, only 1% of new medical devices undergo FDA review of safety and effectiveness.

The recent report of the FDA Committee for Clinical Review (The Temple Report) has found certain patterns of deficiencies in the design, conduct and analysis of clinical studies supporting applications for both substantial equivalence and premarket approval of devices. The deficiencies found by the Committee were sufficiently serious to impede the agency's ability to make the necessary judgements about the safety and effectiveness of the devices in question. Changes recommended by the Committee may improve the quality of data submitted in support of device applications. However, the issue of the large number of new devices cleared only on the basis of substantial equivalency remains. The safety and effectiveness of such devices are not evaluated by the FDA.

RECOMMENDATIONS FOR PROMOTING MEANINGFUL CLINICAL RESEARCH

More rigorous, meaningful clinical research is clearly needed to establish the comparative efficacy of new technologies. Studies are also needed to determine the appropriate uses of technologies determined to be effective, both existing and new. We believe it is appropriate for payers, manufacturers, providers, and clinical researchers to collaborate voluntarily in this clinical research, particularly under health care reform.

Payers historically have not considered clinical research to be within their purview. Insurers paid benefits for technologies know to be effective. However, data on efficacy cannot be developed for some new technologies unless patient care costs of trials are supported. Depending on the type of care involved, patient care costs of research can be very high. Through the Demonstration Project on Breast Cancer Treatment, participating Plans are contributing an average of $67,000 per member transplanted. The research and administrative costs supported by the NCI are $3,000 to $4,000 per case. Patients receiving new investigational treatments may also experience complications that they would not have developed under conventional treatment. The care for such complications will also generate new costs.

Unfortunately, all clinical studies currently conducted are not equal in terms of rigor of design, importance of clinical question addressed, and potential impact on society. Payors cannot be expected to support all clinical research of new technologies. The costs could divert premium dollars away from prevention and other essential services to support unproven technologies. Much of the

research would contribute little to the resolution of scientific questions. Support of clinical research must be voluntary and targeted to high priority, well-designed trials. To accomplish this end, we offer the following recommendations.

- First, we recommend the establishment of a national research advisory board to evaluate and prioritize all the clinical research on new and existing technologies.

  The FDA has processes in place to review safety and effectiveness of new drugs, biologicals, and devices. The National Institutes of Health, Veterans Administration, and other federal agencies have their own review processes for clinical trial funding. The Agency for Health Care Policy and Research (AHCPR) assesses technologies and funds Patient Outcome Research Team (PORT) studies to assess the comparative efficacy of treatments and technologies. However, there is no coordinating body that coordinates these review processes or establishes priorities among clinical research activities.

  There should be a national research board which would develop a national research agenda. Such a board would be charged with weighing the competing needs of different populations and diseases and ranking studies based on the quality of the study and the importance of the trials. The board could be comprised of clinical research experts, practitioners, ethicists and consumers. Such a board is necessary to establish which trials are most important so that studies of new technologies for cancer

and AIDS can be ranked with technologies for alcoholism and Alzheimer's disease.

The national research board should also attempt to estimate the cost of each study. Such cost estimates will help health plans determine which and how many trials they could support within their limited budgets.

- Second, the federal government should develop incentives to encourage health plans to support high priority clinical trials. We do not believe the government should mandate coverage of patient care costs for an investigational technology under evaluation in clinical trials. Patient care costs for certain investigational treatments such as high dose chemotherapy with ABMT support can be very high. Broad coverage of such costs could potentially bankrupt the system and divert resources from the fundamental goal of universal access.

  The following incentives from the federal government would stimulate health plan support of clinical trials:

  - o Tax credits to offset health plan expenditures on high priority clinical trials

  - o Legal protection for health plans exempting them from contract litigation from members who seek access to non-priority trials. Plans need clear protections so that this type of limited support for selected trials cannot be construed as blanket coverage and an

obligation to support all clinical trials.

- Third, manufacturers and researchers would collaborate in this joint research agenda through cost-sharing. When payers support the patient care costs of new unproven technologies, they should negotiate fixed package payments with providers who will also bear some of the costs. Profits or contributions to overhead should be unacceptable on unproven technologies.

Working together, government, payers, manufacturers and researchers can collaborate to evaluate technology and assure access to effective and appropriate medical technology under health care reform.

I. Technology Assessment at BCBSM

II. Technology Review Process at BCBSM

III. Importance of Data and Outcome Studies

IV. Examples of Reviews

- Implantable Cardiac Defibrillator
- Tacrine
- Home Uterine Monitors

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VI. Funding of Research

- Pilot programs

VII. BCBSM/BCBSA Involvement with Professional Organizations

- Minnesota Medical Alley
- BCBSA/Kaiser Permanente Relationship

VIII. Summary

I. Technology Assessment at Blue Cross and Blue Shield of Minnesota (BCBSM)

Affordability of health care in the 1990s is the single overriding concern at BCBSM. We believe the ready acceptance of new technology by providers and the public and its diffusion are major contributors to the cost spiral in health care. New technologies are frequently implemented without addressing the value they add to the continuum of health care and their impact on outcome and cost.

Payers have developed skills in evaluating new, as well as established and outdated medical technologies. BCBSM implemented a medical policy project in 1985 that has eliminated outdated technologies as eligible benefits and formally reviews new drugs, procedures and devices. Five clearly stated criteria must be met before a new technology becomes an eligible benefit. The five criteria are:

1. The technology must have final approval from the appropriate government regulatory bodies.

2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.

3. The technology must improve the net health outcome.

4. The technology must be as beneficial as any established alternatives.

5. The improvement must be attainable outside the investigational settings.

The guidelines were developed by the Blue Cross and Blue Shield Association (BCBSA) with the assistance of Dr. David Eddy and adopted by BCBSM (handout #1).

A sixth criterion is also considered when evaluating a technology and that is cost effectiveness. A technology is cost effective if it is: 1) that which is at least as effective and less costly than alternative technologies, or 2) more effective and more costly than alternative technologies, but the patient outcomes justify additional expenditures, or 3) less effective and less costly than alternative technologies; however, the patient outcome does not justify the additional expenditure.

II. Technology Review Process at BCBSM

BCBSM has committed three full-time staff plus the Medical Director to perform technology assessment. These four individuals meet weekly for two-three hours to discuss new referrals and ongoing technology issues. Issues are brought to the table by soliciting the provider community, vendors, patients, and staff members. We also obtain referrals by reading medical journals, the Wall Street Journal, and our local newspapers.

The technology assessment group discusses and determines if a corporate medical policy is needed (handout #2). If the answer is yes, the research begins. The staff seeks information from the peer-reviewed literature and by consultation with the medical experts locally and nationally. We often begin by requesting more information from the provider (handout #3). Once all the information is obtained, a rationale is created and then presented to the corporate Medical Policy Committee. Experts in the specialty area of review may be invited to come in and discuss the issues or we may visit them on-site at their respective clinics, hospitals or businesses.

The Medical Policy Committee is comprised of:

- five physicians (four who are employed by BCBSM and one who is an external consultant),
- two Medical Affairs Consultants (these staff members are in the technology assessment group),
- three RN's (one RN is the manager of Medical Review/Technology Assessment and serves as the Chairperson, one RN is from the Provider Relations/Contracting Department and one RN is a staff person from the managed care area),
- an attorney from our Subscriber Contract and Compliance Department, and
- a representative from the BCBSM's claims processing department.

This committee meets every three weeks to discuss technology issues and make policy decisions for BCBSM. If a decision cannot be made with the information that is presented, more research will be done and then be presented at the next meeting. This committee evaluates all the evidence that has been made available.

III. Importance of Data and Outcome Studies

Good decisions can be made through the process described above. However, the quality of the decision and the strength of the rationale depend on the availability of data from well-designed clinical trials, data that have been subjected to rigorous statistical analysis, and published in peer-reviewed journals. Stated another way, technology assessment is very effective when the medical literature and expert opinion are unequivocal. When data are limited or nonexistent, the reliability and validity of the outcome of a formal technology assessment can be legitimately challenged. This situation will lead to one or two errors. The first is to pay for a service or product because of public demand without proof that it adds value. The second is to deny payment, causing a number of potential harmful effects such as failure of a small start-up company with displacement of workers, loss of a useful product from the marketplace, and the concomitant negative impact on patient care.

For several years BCBSM has worked closely with the trade association representing the entrepreneurs and larger companies in the health care industry in guiding their research and development to avoid the potential bad decisions mentioned above. We strongly encourage the innovator to begin the process of demonstrating improved outcomes and cost-effectiveness years before its product finds its way into the marketplace. These recommendations are beyond the basic safety and efficacy specifications of the Food and Drug Administration. There are now two levels of review: first the FDA and second, is the value-seeking purchaser. The data requirements of the latter are or will be as stringent as those of the former and certainly as important when managing a budget.

We believe the payer must be a "smart buyer." BCBSM has had a number of opportunities to work with local innovators to help finance the collection of data while making promising new technology available to our members. Most generally, payers have little enthusiasm for such activities due to their tradition of waiting for the data to be accumulated before making a decision rather than financing research and the ability of justifying staff time for the cumbersome administrative activity that supports working with the local companies and innovators. BCBSM fears for its viability in the absence of organized support.

IV. Examples of Reviews

The BCBSM Medical Policy Committee reviews all aspects of technology. The following examples are reviews completed by our staff where data was inadequate and resulted in the following decisions:

1. **Tacrine for Alzheimer's Disease**

(An example where data is insufficient to support reimbursement for the drug)

In July of 1993, the drug tacrine received final FDA approval as treatment for Alzheimer's disease (AD). The results of clinical studies reported in the *New England Journal of Medicine*[1] and the Journal *of the American Medical Association* [2,3] showed that patients receiving the drug demonstrated a mild improvement in certain cognitive functions (such as naming of objects, word recall, attention span) and no significant improvement in problems associated with wandering, verbal and physical outbursts, and sleep disturbance. In each of the major studies, 18% to 25% of subjects withdrew from the clinical trials due to side effects experienced from taking the drug. Discussions with specialists in neurology, psychiatry, and geriatrics also indicated a strong concern for the liver toxicity associated with tacrine's use and a cautionary approach to the issue of how much benefit their patients might realistically expect from this drug.

Based on these findings, BCBSM's Medical Policy Committee made the decision to consider the use of tacrine to be investigative in the treatment of Alzheimer's disease. This decision was based on the following concerns: 1) the results of clinical studies that demonstrated only a mild improvement in patients with respect to certain cognitive functions and no significant improvement in actual functional deficits, 2) no clear identification of those AD patients who would benefit most from treatment with tacrine, 3) the side effect of liver toxicity associated with tacrine's use, and 4) the unpredictable pattern of progression for this disease.

2. **Home Uterine Monitoring (HUM)**

(An example of how poor data quality negatively influenced a reimbursement decision despite the highly important and complex medical problem for which the treatment was designed to improve.)

Uterine contraction monitoring describes an external device, or tocodynamometer, that is used in the home to monitor uterine contractions in pregnant women at risk for premature labor with the intent of decreasing the incidence of premature births. The need to prevent preterm births is critical since the premature infant can experience catastrophic medical problems with costs reaching one million dollars.

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1. Davis KL, et al. A double-blind, placebo-controlled multicenter study of tacrine for Alzheimer's disease. *NEJM*. 1992. 327(18): 1253-1259.
2. Farlow M, et al. A controlled trial of tacrine in Alzheimer's disease. *JAMA*. 1992. 268(18): 2523-2529.
3. Small GW. Editorial - Tacrine for treating Alzheimer's disease. *JAMA*. 1992. 268(18):2564-2565.

The cost of HUM is approximately $5,000 per pregnancy, and an essential component of that care is nursing contact and/or the use of medications. Thus, the important questions we must ask are whether HUM produces healthier babies and whether the additional cost of monitoring pays off.

There is significant controversy concerning the added value of HUM, and support should be found in the clinical trials on HUM. However, after conducting a thorough review of the studies, we found this question was inadequately addressed by the researchers. We found no evidence that the monitoring makes a difference, especially when compared to nursing contact and patient education, the two most common alternatives currently employed. In other words, the benefits of monitoring were not separated from the benefits of nursing care. As a result, improvements in outcome cannot necessarily be attributed to the HUM, and therefore the benefits are unclear. Also, when the alternatives are cheaper, the cost-effectiveness of HUM is unproven.

To date, such a useful, carefully designed study has not been conducted, and the device manufacturers have even turned down requests to participate in one. In the meantime, these home uterine monitoring manufacturers have heavily marketed these devices, producing rapid acceptance and huge revenues generating profits in the millions of dollars. Yet the technology has not undergone critical appraisal prior to widespread use, and the result is millions of health care dollars spent with unproven health benefits. Had the research been designed properly, we may have some answers to a costly medical and social issue that today remains unresolved. Debates such as this will continue until the benefits of competing technologies or treatments are clearly understood.

BCBSM's policy on HUM is that it is investigative, except when used for patients with multiple gestation, between 24 and 35 weeks, with currently diagnosed preterm labor.

3. Implantable Cardioverter Defibrillators (ICD's)

(An example of how we viewed a new technology in the absence of definitive data)

Implantable cardioverter defibrillator (ICD) therapy involves the use of defibrillators that detect and control a variety of life-threatening heart rhythm irregularities, resulting in reduced sudden cardiac death in high-risk patients. ICD technology has rapidly progressed from a treatment of last resort to a primary therapeutic option in some circumstances. This is due to sophisticated technological improvements that have expanded the clinical applications, made them more accepted by patients, and more useful for physicians. However, ICD growth has occurred in the absence of well-designed studies that clearly demonstrate their impact on survival and quality of life. Incidentally, recent trials have reported an increasing incidence of drug failure (the closest alternative therapy) in preventing sudden death.

Long-term studies are not available because ICDs have evolved so rapidly, yet the technological advances inherently offer substantial improvements, which should translate into improved patient outcomes, fewer deaths, improved quality of life, and lower overall costs. In the absence of these data, BCBSM recognized the need to participate in clinical trials with the newer devices since they appeared to offer significant advantages over the existing market-approved devices. However, the

scientific data were in the infancy stage. To assist in gathering the needed data, BCBSM contracted with the Mayo Clinic, a nationally recognized, premiere academic and research institution in our state, which had extensive experience in ICD therapy and high-quality research and good relations with the manufacturers of the newer devices. We agreed to reimburse the device costs, not to exceed the amount payable on an approved device, in properly selected patients. In addition, we are participating in gathering information on short- and long-term costs, device performance, survival, and patient quality of-life-issues.

We believe that participation in these studies is clearly in the best interest of patients, physicians, and the insurer, as well as society at large, if the technology is superior to existing technologies, the health benefits are demonstrated, and financial risk is minimal.

V. Communication to Providers

BCBSM's technology assessment staff publishes a quarterly newsletter to our provider network to keep them informed of new medical policies or revisions to existing ones (handout #4). Once a year, we publish a complete listing of procedures, drugs, and devices that BCBSM considers investigative and ineligible for reimbursement. On a quarterly basis, we then communicate the amendments to this listing.

We find this communication tool a valuable means of keeping in contact with our providers. They are invited to submit additional information to our Medical Policy Committee if they disagree or question our position.

Each policy developed by the Medical Policy Committee is a comprehensive analysis of the scientific literature, following BCBSA's technology evaluation criteria. Presently BCBSM has approximately 300 policies in place and reviews an average of 25 technologies each quarter (handout #5).

VI. Funding of Research

Pilot Programs

At BCBSM, we have found it beneficial to become partners with select providers to research technology. As previously mentioned, we entered into a study with Mayo Clinic and a local manufacturer on the pacemaker cardiac defibrillator after positive experience with other pilots, e.g., laparoscopic cholecystectomy and laparoscopic hernia repair.

These pilot programs assist the manufacturer, physician, and third party payer to facilitate data accumulation when there is great patient demand for a promising technology, then better and wiser decisions can be made in the care of the patient, and net health outcomes.

VII. BCBSM/BCBSA Involvement with Professional Organizations

Minnesota Medical Alley

BCBSM has been an active member of a state organization whose focus is on the health care industry. Medical Alley is "a 225 member trade group whose membership includes high and low technology medical device and product manufacturers, providers of health

care services, third party payers, research facilities, public sector representatives, and those companies and organization which share in the industry's goals and concerns."(4)

Medical Alley is recognized both nationally and internationally for its health-related products, care delivery organizations and professionals, and services. The primary mission is to enhance the operating environments of Minnesota's health care industry.

A task force of Medical Alley members was brought together to develop consensus recommendations to ensure the appropriate adoption and use of medical technology. This committee's document is enclosed (handout #5). BCBSM had representation on this committee and supports the recommendations of this paper.

BCBSA/Kaiser Permanente Relationship

BCBSA recently announced that its Medical Advisory Panel has expanded its membership to include reputable experts in scientific methods, clinical research, and medical practice. Some of the largest physician groups representing internists (the American College of Physicians), family physicians (the American Academy of Family Physicians), and pediatricians (the American Academy of Pediatrics) are now represented on the advisory panel. However, a majority of the panel at BCBSA continues to be independent medical experts with no affiliation with health care payers.

Also, in September 1993, BCBSA signed a cooperative agreement with Kaiser Permanente. This association between BCBSA and Kaiser signals a major collaborative effort, making the Association's TEC program available to Kaiser Permanente and others in the health care industry.

Until this recent agreement, the TEC program assessments were available to other Blue plans only. "As part of the TEC program's expansion, assessments will be offered on a subscription basis to all interested parties, including health care payers, managed care companies, physicians, medical research institutions and libraries." (5)

Over the last two years, BCBSM has also diversified its technology assessment program. Through Comprehensive Managed Care (CMC), a BCBSM affiliate, our managed care and technology assessment staff expertise are contracted out to other payers and managed care companies. Most payers agree that technology assessment is essential; however, they themselves do not have the staff or expertise to perform these functions.

BCBSM has established positive relationships with these other companies and evaluates the technologies that are pressing concerns for payers in their own medical communities. In some cases, they want us to review a technology from its infancy, or they may adapt what we currently have as policy.

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4. Medical Alley news release 1993.
5. Blue Cross and Blue Shield Association press release, September 1993.

VIII. Summary

The value of technology is highly subjective in the absence of data that establishes two essential factors that must be included in the decision. These factors address the impact of a technology on patient outcomes, and the cost effectiveness of a technology compared to alternatives.

A role government may play would be in the establishment of standards for research design, data acquisition, and data reporting. An example of where federal standards have been set is the Institute of Medicine document outlining the essential characteristics of medical care guidelines.

Rigid and premature judgments about the value added of a new technology or new application of an existing technology could easily have a negative impact on patient care, the viability of innovative small firms, and the loss of valuable products from the marketplace.

Financial incentives to those firms engaged in research and development would be desirable. Just how desirable would depend on the structure adopted to implement such a strategy. Again, we believe that education of those involved in innovation through their trade organizations, the setting of standards, and appropriate financial incentives would be desirable.

It is essential that all stakeholders work toward a common goal of financial support for continued development and sensible diffusion of cost effective health care technology.

Handouts

1. BCBSA Technology Assessment Criteria
2. BCBSM technology review process
3. BCBSM provider questionnaire
4. BCBSM quarterly Medical Policy Update
5. Listing of BCBSM medical policies
6. Minnesota Medical Alley task force document

BlueCross BlueShield of Minnesota

P.O. Box 64560 • St. Paul, Minnesota 55164-0560

NATIONAL ASSOCIATION TECHNOLOGY ASSESSMENT CRITERIA

The first step in determining eligibility of a medical procedure for coverage is evaluating its health effects, a process known as technology assessment. The Blue Cross and Blue Shield Association conducts such assessments of selected technologies. The Association's role is informational. Each Blue Cross and Blue Shield Plan makes its own coverage decisions. Plans may consider assessment results in their coverage decisions and any additional factors they may deem appropriate.

The Blue Cross and Blue Shield Association uses the criteria below to determine whether a technology improves health outcome such as length of life, ability to function or quality of life. Technologies that meet all five of the following criteria are recommended for coverage consideration.

1. **The technology must have final approval from the appropriate government regulatory bodies.**

   - A device, drug or biological product must have Food and Drug Administration approval to market for those specific indications and methods of use that Blue Cross and Blue Shield Association is assessing.
   - Approval to market refers to permission for commercial distribution. Any other approval that is granted as an interim step in the FDA regulatory process, e.g., an Investigational Device Exemption, is not sufficient.

2. **The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.**

   - The evidence should consist of well-designed and well-conducted investigations published in peer-reviewed journals. The quality of the body of studies and the consistency of the results are considered in evaluating the evidence.
   - The evidence should demonstrate that the technology can measure or alter the physiological changes related to a disease, injury, illness or condition. In addition, there should be evidence or a convincing argument based on established medical facts that such measurement or alterations affects the health outcomes.
   - Opinions and assessments by national medical associations, consensus panels or other technology assessment bodies are evaluated according to the scientific quality of the supporting evidence and rationale.

3. **The technology must improve the net health outcome.**

   - The technology's beneficial effects on health outcomes should outweigh any harmful effects on health outcomes.

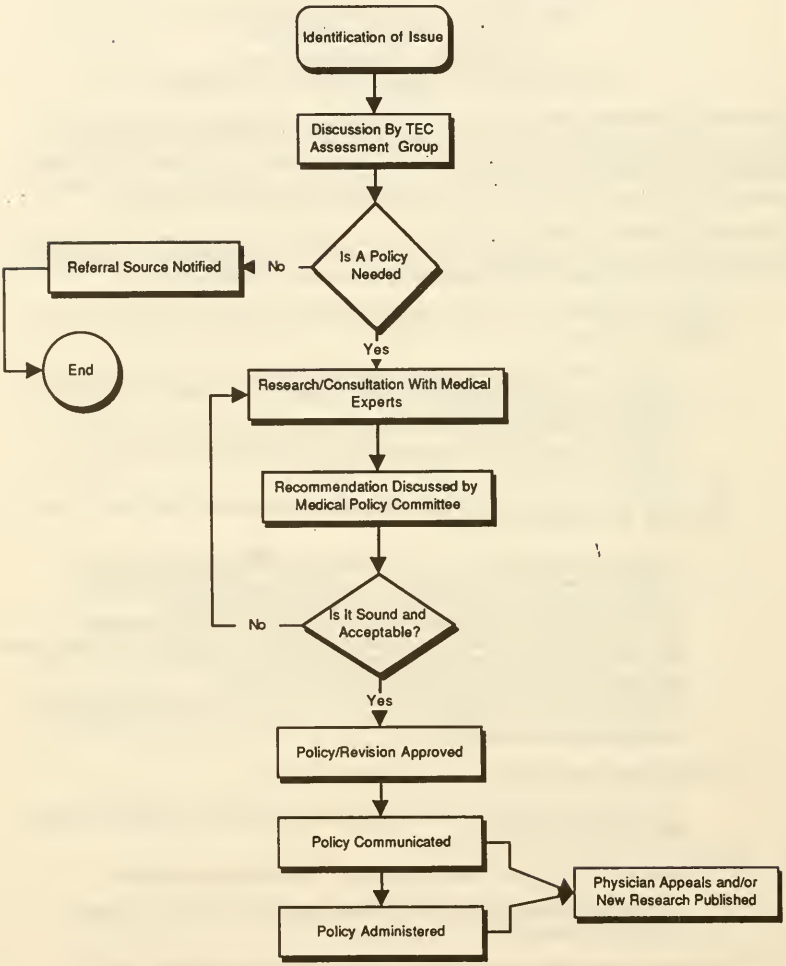
4. **The technology must be as beneficial as any established alternatives.**

   - The technology should improve the net health outcome as much as or more than established alternatives.

5. **The improvement must be attainable outside the investigational settings.**

   - When used under the usual conditions of medical practice, the technology should be reasonably expected to satisfy criteria 3 and 4.

Medical Policy Development



PROVIDER: TECHNOLOGY ASSESSMENT DOCUMENTATION

Provider: _____

Address: _____

Phone: _____

1. Description of technology:

2. What are the criteria patients must meet before they can become candidates for use of this technology:

3. What are the specific indications and methods of use for which this technology has received FDA market approval:

4. How would this technology benefit patients' health outcome:

5. Indicate relevant peer-reviewed journal references which demonstrate the efficacy and safety of this technology:

6. What medical associations, consensus panels, and/or other technology assessment bodies have evaluated the safety and efficacy of this technology:

7. How would the health outcomes using this technology compare to the available alternatives:

8. What would be the fixed and variable costs of this technology:

9. How would the cost of this technology compare to the alternatives:

10. What would be this technology's estimated yearly volume of use:

11. Do you have any financial interest in this technology:

BlueCross BlueShield of Minnesota

Medical Policy

Update

January 1993

MRI - BREAST

MRI of the breast is considered INVESTIGATIVE. Providers submitting claims for this procedure should use CPT code 71550.

COLONY STIMULATING FACTORS

Providers no longer need to prior authorize the use of colony stimulating factors (G-CSF, GM-CSF) for the treatment of febrile neutropenia in patients with non-myeloid malignancies receiving myelosuppressive chemotherapy. Colony stimulating factors are considered INVESTIGATIVE when used in the treatment of HIV, since they have not received FDA approval for this indication.

STEREOTACTIC BREAST BIOPSY

Charges for stereotactic guidance used for performing a breast biopsy should be billed with the following CPT Codes:

75989 - radiologic guidance for specimen collection, radiologic supervision and interpretation
19100 - biopsy of breast; needle

Modifiers:
When the biopsy is performed in a clinic or office setting, no modifiers are required.
When the biopsy is performed in the hospital setting, a -26 modifier should accompany the physician's bill.

QUESTIONS ?

Call BCBSM's Medical Review Department at (612) 456-8502 or (800) 382-2000, ext. 8502.

RESPIRATORY REHABILITATION

BCBSM will continue to reimburse for individually submitted medical services that are a necessary part of a subscriber's respiratory care, rather than reimbursing a global fee for a comprehensive respiratory rehabilitation program.

Although the available published research on respiratory rehabilitation points to improvements among participants in the areas of respiratory function testing and awareness of disease, the research does not show cost effectiveness in terms of reduced hospitalization and ER visits. Lack of this type of evidence influenced the decision to reimburse those individual services deemed to be medically necessary, rather than reimburse for a complete program whose content and presentation will vary from one institution to another. In establishing this method of coverage, we trust that providers will avoid duplication of services and that only those tests and procedures determined to be medically necessary will be submitted for reimbursement.

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NATIONAL BREAST CANCER PREVENTION TRIAL - TAMOXIFEN

Medically eligible BCBSM subscribers who are interested in participating in the National Breast Cancer Prevention Trial using Tamoxifen may be eligible to receive coverage for some medical costs associated with the trial. Subscribers who have received approval for participation in the study by a physician or institution conducting the study are encouraged to request benefit verification in writing, addressed to the Consumer Service Center at BCBSM.

Benefits for the scheduled medical care will be provided according to the subscriber's contract, and they are subject to specified screening benefits, deductibles, co-pays, etc. Since the Tamoxifen used by study participants is provided free of charge by the National Cancer Institute, BCBSM does not expect to be billed for the drug.

Please use ICD-9 diagnosis code V76.1 when submitting charges for the scheduled medical care during the study (i.e., mammograms, x-rays, blood work).

For additional information concerning the trial, you or your patients may call 800-225-2268.

BCBSM DEMONSTRATION PROJECT FOR BREAST CANCER

Blue Cross and Blue Shield of Minnesota subscribers may be eligible to participate in a clinical trial of high dose chemotherapy with autologous bone marrow rescue (HDC/ABMR) for the treatment of breast cancer.

The Blue Cross and Blue Shield Demonstration Project on Breast Cancer Treatment supports four randomized clinical trials comparing the efficacy of HDC/ABMR to conventional chemotherapy in the treatment of breast cancer. This initiative is sponsored by the National Cancer Institute (NCI), the Blue Cross and Blue Shield Association, 15 Blue Cross and Blue Shield Plans, and the Blue Cross and Blue Shield Federal Employee Program.

HDC/ABMR for the treatment of breast cancer is not covered by Blue Cross and Blue Shield of Minnesota at this time. However, the Demonstration Project provides financial support to participating institutions on behalf of our subscribers who receive HDC/ABMR through one of the four randomized clinical trials.

Currently, there are 40 bone marrow transplant centers nationwide participating in the Demonstration Project. These institutions are members of cancer Cooperative Groups conducting the trials. Only those institutions that are members of a Cooperative Group and have signed an agreement to participate in the Demonstration Project may receive payments for HDC/ABMR through the project.

We encourage you to consider the Demonstration Project prior to the initiation of treatment for breast cancer.

For information regarding patient eligibility criteria, contact James E. Radford, Jr., M.D. (612) 624-7984 at the University of Minnesota Hospital and Clinic or James N. Ingle, M.D., (507) 284-4849 at the Mayo Clinic.

Information on referring Blue Cross and Blue Shield of Minnesota subscribers and subscribers on the Federal Employee Program to the Demonstration Project may be obtained by calling 1-800-225-2268.

Information on referring non-Blue Cross and Blue Shield patients may be obtained by calling the NCI information number, 1-800-4-CANCER. You may also call the Cooperative Groups directly.

CALGB	603-650-6270
ECOG	608-263-6650
SWOG	512-366-9300
Philadelphia BMT Group	215-662-6394

Thank you for taking the time to consider clinical trial participation for Blue Cross and Blue Shield of Minnesota subscribers suffering from breast cancer.

CORRECTIONS

Gundersen Lyme Test - As stated in the September issue, providers submitting claims for the Gundersen lyme disease test should use code 06699. This code is a BCBSM internal specialty code, not a CPT code.

Vision Therapy (92065) - Does NOT require prior authorization.

Nicotine Dependence - Individual counseling services related to smoking cessation provided to healthy patients by a physician should be billed as follows:
ICD-9 code: V65.4
CPT codes: 99401-99404

GASTRIC BYPASS/GASTROPLASTY

Morbid obesity is associated with a reduction in life expectancy and significant co-morbid medical and psychological conditions. Surgical intervention is considered a form of risk reduction in morbidly obese patients with serious medical problems, although there is no long term data to support survival benefit. The decision to undergo surgical intervention is shared by the physician and patient and is based on factors such as the patient's present weight, weight loss history, physical and mental readiness, patient expectations and motivation, all of which are determined by a qualified team of professionals with integrated knowledge of medicine, surgery, psychiatry, nutrition and exercise.

The newly revised eligibility criteria for gastric bypass procedures are as follows:

A. Approval Criteria:

1. The patient must weigh at least 100 pounds more than the upper figure range in the medium frame category of the Metropolitan Life Insurance Table of Desired Weights.

2. The excess weight must be of at least five years duration. The prior authorization request must include the following information:
   a. Documented weights for the last 5 years in physician records; and
   b. Personal weight history/patterns including duration of obesity; and
   c. Immediate family history of morbid obesity.

3. The patient must have actively participated in non-surgical methods of weight reduction, and these efforts must be fully appraised by the physician requesting authorization for surgery.
   Note: It is the responsibility of the physician to refer the patient preoperatively to qualified professionals for diet counseling and a medically supervised weight loss program if prior attempts are deemed inadequate or are absent.

4. The physician must certify that the patient's psychiatric profile is such that the patient is able to understand, tolerate and comply with all phases of care and is committed to long term follow-up requirements.
   Note: It is the responsibility of the primary team physician to refer the patient at any time before or during treatment, as deemed necessary, for consultative interaction with a Licensed Consulting Psychologist or Psychiatrist for assessment, treatment and/or follow-up care of psychosocial needs.

5. The patient should receive from the physician a thorough explanation about the risks, benefits and uncertainties of the proposed procedure.

B. Re-operation Criteria:

Subsequent surgery for morbid obesity to correct a technical failure or to repair a complication is subject to contract-specific eligibility requirements. Some contracts exclude coverage for repeat bariatric surgery and related expenses.

If contractually eligible, the patient must meet the following criterion in addition to criteria A.4 and A.5 above.

1. Technical failure of primary operation:
   a. Staple line disruption - documented by x-ray, or
   b. Expanded outlet - documented by gastroscopy, or
   c. Enlarged anastomosis - documented by gastroscopy.

Prior authorization is required for all bariatric surgery and revisions/reoperations. Panniculectomy following gastric bypass procedures is considered cosmetic, even when performed incidentally to a diastasis recti repair, and it is therefore contractually ineligible.

January 1993

Investigative List

Ablation, (Catheter) - investigative except for:

1. Radiofrequency - for modulation of AV nodal reentrant tachycardia (SVT), and for ablation of accessory pathways (Wolff-Parkinson-White)
2. Direct current - for ablation of the AV node in atrial fibrillation-flutter.

Catheter ablation of ventricular tachycardia foci is considered investigational.

Acupuncture - investigative except for anesthesia administered by a physician.

Acuscope

Airway Stents - The use of short term stents in the treatment of acute traumatic injury is considered accepted medical practice. The use of long term endobronchial stents in the treatment of severe airway tracheal and/or bronchial malacia is considered investigative.

Allergy Testing and Treatment - including but not limited to:

A. Testing

1. Cytotoxic Leukocyte Testing (Bryan's test) NOTE: This is different from leukocyte immunizations;
2. Leukocyte Histamine Release Testing;
3. Provocation - Neutralization Testing (sublingual, intracutaneous or subcutaneous);
4. Rebuck Skin Window Test;
5. Passive Transfer or P-K Test;
6. Candidiasis Hypersensitivity Syndrome Testing;
7. IgG Level Testing (IgG level testing for immunodeficiency is eligible for coverage)
8. General Volatile Organic Screening Test for Volatile Aliphatic Panel.

B. Treatment

1. Provocation - Neutralization Treatment for Food Allergies (sublingual, intracutaneous and subcutaneous);
2. Rinkel Immunotherapy (Serial Dilution Endpoint Titration); Note: Allergy testing using this method is eligible as a variant of conventional intradermal skin testing.
3. Autogenous Urine Immunizations;
4. Clinical Ecology Units;
5. Candidiasis Hypersensitivity Syndrome Treatment;
6. IV Vitamin C Therapy;

Alloplastic Spermatocele

Alpha- 1 Antitrypsin Deficiency Replacement Therapy - investigative except when used in patients satisfying the following criteria:

1. inherited alpha- 1 antitrypsin deficiency;
2. nonsmoking;
3. forced expiratory volume (FEV_1) should be less than 65% of the normal value;
4. patients waiting for lung transplantation.

Amalgams - the replacement of amalgams (dental restorations) due to any assertion of mercury allergy, poisoning, etc. is considered investigative.

Ambulatory Blood Pressure Monitoring

Angelchik Anti-Reflux Prosthesis

Angioplasty, Laser

Angioscopy

Anorectal Physiology Testing - the following tests should be considered investigative:

1. balloon proctography;
2. scintigraphic assessment of expulsion or anorectal angle;
3. colon transit studies using radio-opaque markers;
4. axial force probe;
5. rectal barostat;
6. whole anal canal pressure profile.

Antisperm Antibody Tests -investigative except when used for the following:

1. autoagglutination of sperm;
2. infertile couples with poor results in the postcoital test or Huhner test;
3. in couples with unexplained infertility (all other causes have been ruled out);
4. in follow-up testing, if immunosuppressive therapy (steroids) are initiated at sub maximal doses (i.e., less than 96 mg. methylprednisolone per day).

Apheresis - Apheresis includes plasmapheresis (P), erythrocytapheresis (E), leukocytapheresis (LE), lymphocytapheresis (LY), and thrombocytapheresis (T). It is investigative except for the following conditions:

Dermatologic
- Pemphigus vulgaris; refractory (P)

Hematologic
- ABO-incompatible bone marrow transplantation (P)
- Coagulation factor inhibitors (hemophilia, nonhemophilia): Failed conventional therapy, significant hemorrhage, or planned elective surgery (P)
- Hemophilia with factor VIIIc inhibitors: Failed conventional therapy, significant hemorrhage, or planned elective surgery (P)
- Hyperviscosity syndrome (P)
- Leukemia: Acute debulking or blast crisis (LE)
- Leukemia: chronic myelogenous (CML) (LE)
- Leukemia: Hairy-cell (LE)
- Maternal fetal incompatibility: High risk of fetal demise, and early delivery or intrauterine transfusion is not possible (P).
- Multiple myeloma: renal failure (P)
- Post-transfusion purpura (P)
- Sickle-cell disease (E)
- Thrombotic thrombocytopenic purpura (TTP) (P)
- Thrombocytosis: symptomatic or presurgical (T)
- Waldenstrom's macroglobulinemia (P)

Metabolic Disease
- Hypercholesterolemia: Familial type IIA homozygous form (P)
- Hyperlipoproteinemia: Familial type IIA homozygous form (P)
- Refsum's disease (P)

Cold Laser Treatment for pain relief or healing is considered investigative. Collagen Injections/Implants when used for podiatric procedures.

Colony-Stimulating Factors - investigative except when used for the following:

1. G-CSF (Neupogen®, Filgastim®): as treatment to decrease the incidence of infection, manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive chemotherapy drugs that are associated with a significant incidence of febrile neutropenia.
2. GM-CSF (Prokine®, Leukine/Sargramostim®): in patients with non-Hodgkin's lymphoma, acute lymphoblastic leukemia, and Hodgkin's disease undergoing autologous bone marrow transplantation.

Note: Any other use of the above colony-stimulating factors is considered investigative. The use of any other colony-stimulating factor is considered investigative.

Coma Stimulation Programs

Cordocentesis, Percutaneous Umbilical

Coronary Angioscopy

Cranial Sacral Therapy

CT Generated Orthopedic Models (Orthoscan)

Cytoxan for Neurological Disorders - investigative except in patients with progressive MS who have failed standard therapy.

Defibrillator (home)

Dental (Endoseous) Implants - investigative except for the Branemark system used for fully edentulous patients. NOTE: They are only covered under the AWARE Dental contract, not under the standard Blue Cross Blue Shield contract.

Dermabrasion for Acne (considered cosmetic or investigative, depending on clinical stage of acne).

Doppler Velocity Probe (cardiac)

DNA Probes - investigative except when used for the following indications:

1. Infectious diseases (CPT codes 87178, 87179) caused by:
   a. Chlamydia
   b. Mycobacterium
   c. Neisseria gonorrheae
   d. Mycoplasma pneumoniae
2. Genetic diseases (CPT codes 83912, 83913)
   a. Cystic fibrosis
   b. Duchene's muscular dystrophy
   c. Fragile x syndrome
   d. Retinoblastoma
3 Hematologic diseases (CPT codes 83912, 83913)
   a. Chronic myeloid leukemia
   b. Acute myeloid leukemia
   c. Acute lymphoblastic leukemia

Dual Energy Absorptiometry (Bone Mineralization Study)

ECG, Variance Electrocardiography

Electro-Dental Evaluation

Electrodiagnostic Machines used in homeopathic medicine are considered investigative.

Endoscopy, Vascular

Energy Emission Analysis

Epikeratophakia Lens (prior authorization required for eligible indications).

ERGYS

Esophageal pH Monitoring - investigative except:

1. in patients who have documented noncardiac induced chest pain;
2. to rule out reflux induced pulmonary disorders in patients who have recurrent respiratory symptoms;
3. in patients who have been unresponsive to medical therapy or surgery.

Extracranial - Intracranial Arterial Bypass (Anastomosis) - investigative except when used to treat patients requiring either extended temporary or permanent proximal occlusion of major intracranial vessels while treating other types of pathology.

Fallopian Tube Catheterization

Gastric Bubble/Balloon

Gastric Motility Studies - this includes gastrointestinal manometry, electrogastrophy, intraoperatively or surgically implanted electrodes.

Gastrogram

Gene Therapy

Gunderson Lyme Test - test is considered investigative. Providers wishing to submit claims should use code 06699.

Hair Analysis

Histamine Therapy - investigative except when used for treatment of cluster headaches.

Homeopathy and Homeopathic Treatments/Drugs - (also see IV Minerals and Vitamins)

Hormone Pellets - investigative for home use.

Hyperbaric Oxygen Therapy (prior authorization is required for eligible indications).

Hyperthermia Therapy - investigative except for local hyperthermia in combination with radiation therapy in patients who have failed previous therapy or are not candidates for conventional treatment.

Hypnotherapy for Anesthesia

Immunoglobulin Therapy - investigative for the treatment of multiple sclerosis, chronic fatigue syndrome, and demyelinating polyneuropathy.

Immunotherapy and Immunological Testing - immunological testing in the treatment of RSA is considered investigative.

Impotence - surgical correction of organic impotence by either venous or arterial procedures is considered investigative.

Infusion Pumps (Implantable) - investigative except when used for the following indications:

A. Arterial access (CPT codes 36260, 36261)

1. Colon and rectal cancer with metastasis confined to the liver;
2. Unresectable carcinoid tumors of the liver;
3. Primary liver cancer;

B. Epidural access (CPT codes 63750, 63780)

1. Administration of analgesia for control of severe, intractable pain of the terminally ill secondary to malignancy;
2. Control of spasticity with low dose morphine;
3. Control of physically disabling spasticity of spinal origin (i.e., resulting from Multiple Sclerosis or spinal cord injury) with intrathecal baclofen (Lioresal®) in patients who:
   a. are refractive to various pharmacologic (i.e., oral baclofen) and exercise therapies, and
   b. have a significant functional component that is expected to improve with this therapy.

Note: We will pay for services associated with infusion pumps only when the pump is FDA approved. These associated services include implantation surgery and hospitalization. All other uses of infusion pumps are to be considered investigative, including control of spasticity with the drug Lioresal (Baclofen).

Interferential Home Therapy Devices - investigative except when physical therapy treatment modalities are ordered by a physician and performed by a physical therapist in the office/clinic setting; it is reimbursed under CPT 97014.

Interferon - investigative for all diagnoses except for the treatment of hairy-cell leukemia, AIDS-related Kaposi's sarcoma, condylomata acuminata, and hepatitis C (non-A, non-B hepatitis), and chronic granulomatous disease.

Interleukin 2

Intravaginal Conception (IVC)

Iontophoresis Devices for Hyperhidrosis

IV Vitamins and Minerals - investigative when administered in the office setting for allergies, candidiasis, chronic fatigue syndrome, Epstein-Barr virus, and multiple sclerosis.

Keratimilusis - investigative except for:

1. for a person with congenital cataracts;
2. for a patient with keratoconus;
3. rarely for patients who cannot wear any type of corrective lenses and are not suitable for an implant and for patients whose occupation is not conducive to other forms of corrective lenses;
4. for patients with significant corneal scarring associated with severe visual impairment in whom a corneal graft is functionally less desirable.

Note: Prior authorization is required for eligible indications.

Laparoscopic Hiatal Hernia Repair (Nissen Fundoplication)

Laparoscopic Selective Vagotomy

Laser Corneal Sculpturing

Laser Percutaneous Lumbar Discectomy

Laser Transurethral Resection of the Prostate

Light Reflection Rheography

Limb Perfusion (isolated)

Lithotripsy for Treatment of Gallstones

Live Cell Analysis

Lixiscope

Lyme Borreliosis Antigen Testing

Lymphokine Activated Killer Cells (LAK)

Magnetic Resonance Imaging - MRI of the chest, myocardium, breast glenoid labral abnormalities, humoral head fractures, glenoid fractures, glenoid capsular stripping, and arthritic shoulders are considered investigative. MRI for angiography is also considered investigative.

Meniscus Transplants

Methyl Tert - Butyl Ether (MTBE)

Monoclonal Antibodies - investigative except for Orthoclone, OKT-3 for acute rejection of kidney transplants.

Nerve Expansion

Neurometer

Neutron Beam Therapy - investigative except for treatment of an unresectable cerebral aneurysm.

Pacemaker Cardioverter Defibrillator

Partial Ileal Bypass - investigative except when performed for patients with:

1. diagnosis of heterozygous type IIa hypercholesterolemia (defined as LDL 190 with normal triglycerides), and
2. failure of diet and drug treatment. Treatment failure must be defined by a specialized center in lipid disorders.

Percutaneous Cardiopulmonary Support (PCPS)

Percutaneous Nephrectomy

Perrymeter

Photodensitometry (Bone Mineralization Studies)

Photodynamic Therapy

Photopheresis - investigative except for the treatment of cutaneous T-cell lymphoma. (The use of photopheresis for the treatment of scleroderma is considered investigative.)

Phototherapy Lights - investigative for Seasonal Affective Disorders (SAD).

Physiological Stress Test Hemodynamics

Platelet Derived Wound Healing Factor (PDWHF)

Plethysmography, Bioelectric Impedance

Positron Emission Tomography (PET Scan) - investigative except when used for localization of epileptogenic focus in patients with complex partial epileptic seizures who have failed to respond to medical therapy and who are being considered for surgery. Prior authorization is required.

Posturography

Prolastin™ - see alpha- 1 antitrypsin deficiency for indications for coverage.

Prolotherapy

Promontory Test

Prostate Specific Antigen (PSA) - investigative except when used in follow-up of documented diagnosis of prostate cancer. See attached position paper.

Prostatron

Prostatic Acid Phosphatase (PAP) - investigative except when used in follow-up of documented diagnosis of prostate cancer.

Protirelin - investigative except:

1. to test pituitary, hypothalamic and thyroid function;
2. for treatment of last resort for infantile spasms.

Protropin - Inpatient admission for provocative testing is considered not medically necessary. Individual cases with documented extenuating circumstances which may warrant an inpatient stay will be considered (growth hormone). Prior authorization is required.

Quantitative Computed Tomography (Bone Mineralization Studies)

Radiogrammetry (Bone Mineralization Studies)

Retin-A (Topical Tretinois Treatment) - investigative except when used to treat acne vulgaris and selected disorders of keratinization including lamellar ichthyosis and Darier's disease.

Rhinomanometry

Rhizotomy - investigative except for the treatment of patients with cerebral palsy, spinal cord injury, and selected cases of traumatic brain injury. Prior authorization is required for eligible indications.

Rotating Chair Test

Sclerotherapy - investigative as a stand-alone treatment for varicose veins of the lower extremities. Sclerotherapy used in conjunction with surgical ligation or stripping, up to four months postoperatively, is considered accepted medical practice. Prior authorization is required.

Seismocardiogram

Signal-Averaged ECG

Silicone Injection - investigative when used for podiatric procedures.

Single Photon Absorptiometry (Bone Mineralization Studies)

Somatostatin Analog - investigative except for the treatment of metastatic carcinoid tumors and vasoactive intestinal peptide-secreting (VIP) tumors.

SPECT Imaging - investigative except when used for the following indications:

1. heart (cardiovascular functions);
2. lymphoma.

Sperm Penetration Assay - investigative except when used for the following indications:

1. to determine the advisability of artificial insemination by donor or husband;
2. to determine the advisability of in-vitro fertilization by donor or husband;
3. to determine the advisability of varicocelectomy in patients with unexplained infertility, normal semen analysis, and varicocele.

SpineTrak

Stereotactic Interstitial Irradiation of Malignant Brain Tumors

Stereotactic Radiosurgery - investigative except when it is used as an alternative to open surgery, when the device being used is FDA approved specifically for stereotactic radiosurgery, and when one of the following conditions exist:

1. patient's lesion is located in a deep, inaccessible, or complex brain region where the risk of surgical removal is deemed unacceptable; or
2. patient's medical condition poses unacceptable risk for conventional surgical removal.

Tai Chi Ch'uan

Temporomandibular Joint (TMJ) Disorder and Craniomandibular Joint - the following are considered investigative when used in the diagnosis and treatment of TMJ and craniomandibular disorders:

1. electromyography (EMG) (CPT codes 95867, 95868)
2. computerized mandibular scanner (CPT code 97752)
3. computerized jaw tracking/motion analysis (CPT code 97752)
4. doppler auscultation
5. sonography/ultrasound (CPT codes 76066, 76999, 78380)

Therastim

Thermography

Tissue Type Plasminogen Activator (TPA) -investigative except when used as intravenous administration for cardiac thrombolysis during management of an evolving acute myocardial infarction.

Topical Hyperbaric Oxygen Treatment - for home use

Topographic Brain Mapping

Transcranial Doppler Ultrasound - investigative except when provided for the following indications:

1. detecting severe stenosis in the major basal intracranial arteries;

2. assessing patterns and extent of collateral circulation in patients with known regions of severe stenosis or occlusion;
3. evaluating and following patients with vasoconstriction of any cause especially after subarachnoid hemorrhage;
4. detecting arteriovenous malformations and studying their supply arteries and flow patterns;
5. assessing patients with suspected brain death.

Transperineal Injections for Chronic Prostatitis

Transrectal Ultrasound - investigative except for preoperative staging of known colorectal carcinomas. It is accepted medical practice, but not medically necessary, when used to guide a prostate biopsy, therefore, separate reimbursement for the ultrasound is not eligible, as it is considered part of the biopsy procedure.

Tubal Cannulation - investigative when used for performing assisted reproductive procedures and managing ectopic pregnancy.

Tumor Cell Sensitivity Assay

Tumor Markers: (Δ See specific tumor marker policy for approved indications)

1. CA 15-3
2. CA 19-9

Δ 3. CA 125
Δ 4. CEA
Δ 5. PAP
Δ 6. PSA

Ultrasonic Valvuloplasty

Uterine Contraction Monitor (Home)

Uterine Lavage for Preembryo Transfer

Variance Cardiography

Vascular Surgery for Impotence - surgical correction of organic impotence by either venous or arterial procedures is considered investigative.

Ventricular Assist Pumps

TOPICS CURRENTLY UNDER REVIEW

Autonomic Function Testing
Extracorporeal Membrane Oxygenator (ECMO)
Flow Cytometry
Home Uterine Monitoring
Interleukin-2
Percutaneous Cardiopulmonary Support
Protropin in Turner's Syndrome and other GH nondeficient states
Rhinoplasty
Ventricular Assist Pumps

January 1993

Medications/Procedures/Services Requiring Prior Authorization

Ablation, endometrial

Apnea Monitoring (infant)

Artificial Insemination

Assisted Reproductive Technologies (invitro fertilization, GIFT, ZIFT, frozen embryo transfer, etc.)

Autograft Skin Culture and Culture Transplants

Balloon Valvuloplasty of the Aortic Valve - generally considered investigative - each case will be reviewed on its own merit

Blepharoplasty (upper lids only - lower lids are considered cosmetic)

Bone Growth Stimulators

Bone Marrow Transplantation

Breast Implant Removal and/or Insertion

Cardioverter Defibrillator - Implantable

Cochlear Implantation

Diastasis Recti Repair

Dorsal Column Stimulation

Durable Medical Equipment (apnea monitors, compression vests, Hoyer lifts, wheelchairs, lift chairs, ultraviolet lights for psoriasis, hospital beds and items that are purchased over $700)

Endometrial Ablation

Epikeratophakia

Erythropoietin

Event recordings (infant)

Gastric Bypass/Gastroplasty

Growth Hormone (Protropin, Somatrin, Humatrope)

Gynecomastia (Prior authorization is required for this procedure when the treating physician feels there is a medically necessary reason for performing the surgery. If a prior authorization is not on file when a claim is submitted, BCBSM may assume that the physician has determined the surgery to be cosmetic in nature and has discussed this with the patient. The subscriber contracts indicate that cosmetic procedures are ineligible for reimbursement).

Home Health Agency Services

Hyperbaric Oxygen Therapy (in-home therapy only)

Infertility Drugs (injectable)

Implantable Infusion Pumps

Keratimilusis

Mastectomy, Prophylactic - a psychiatric evaluation is required for patients seeking mastectomy for diagnosis of mastodynia

Mastectomy, Subcutaneous

Mastopexy

Medication Management for Outpatient Mental Health (exceeding 12 half-hour sessions)

Oophorectomy, Prophylactic

Organ Transplants (heart-lung, heart, liver, pancreas, kidney-pancreas, and lung)

Pain Rehabilitation Programs - outpatient only

Palatopharyngoplasty

Partial Ileal Bypass

Percutaneous Lumbar Discectomy (Lumbar Discectomy - Percutaneous)

Pergonal Therapy

Polysomnography

Port Wine Stain, Dye Laser Treatment

Positron Emission Tomography (PET Scan)

Radial Keratotomy or other refractive error correction surgery

Reconstructive Surgery (Breast)

Reduction Mammoplasty

Rhinoplasty

Rhizotomy

Scar Revision/Revision after surgery

Sclerotherapy

Sleep Disorder Diagnostic Testing - A consultation report from either the referring physician or sleep disorder center must accompany the prior authorization. This will be requested if it is not submitted.

Suction Lipectomy

Temporomandibular Joint (treatment)

Uvulectomy

Uvulopalatopharyngoplasty

Vest Percussor

Weight Reduction Programs

Photographs required
* New to prior authorization list

Note: We do not encourage or require prior authorization requests for obviously covered procedures and surgeries. The above services require prior authorization, and this does not necessarily mean that they are considered investigative.

BCBSM Position on Prostate-Specific Antigen (PSA)

Disease

Prostate cancer is the second most common form of cancer (second to skin) and the second most common cause of cancer deaths in men in the United States. In 1992, it is estimated that 132,000 new cases will be diagnosed nationwide (2,600 in MN), and 34,000 men will die from the disease nationwide (650 in MN)(1). The increasing incidence may be due in part to the aging population (incidence increases with age), greater frequency of screening, and improved cancer registration. However, death rates from prostate cancer have risen slightly since 1949 (US Preventive Services Task Force).

Between 40-85% of tumors have spread beyond the prostate at diagnosis. This is associated with higher mortality. However, it is estimated that only 1 in 380 men with histological manifestation of prostate cancer actually die from the disease. The ability to distinguish between men who are likely to die from the disease if untreated from those who may live with it unaffected remains unestablished. Efforts remain focused on early detection of localized disease with the goal of reducing disease-associated mortality.

Position

Our current position is that PSA is accepted medical practice when used to detect and treat subclinical prostate cancer recurrence or residual disease in previously diagnosed and treated patients. Detectable PSA levels after prostatectomy indicate the presence of residual prostate tissue or disease. Rising PSA levels after radiation or hormonal therapy indicate disease progression and treatment failure. All other uses are investigational including its use as a screening tool for latent carcinoma.

Screening

Screening is defined as testing persons with neither evidence nor risk factors for a specific disease (BCBSA Screening Guidelines). Disease prevention and detection are appropriate factors in health care promotion, but BCBSM seeks to reimburse for services known to improve health outcomes. The primary goal of any cancer screening program should be to reduce disease-specific mortality (2). The rationale behind screening for prostate cancer is that slowly growing cancers, if detected early, can be effectively treated and cured; and the efficacy of such is measured by a resulting decline in morbidity and mortality. Improved survival has not been demonstrated for this disease, therefore the value of mass screening for prostate cancer is unestablished.

The use of PSA as a stand-alone screening tool is neither widely accepted nor recommended by acknowledged medical experts or the FDA due to its poor sensitivity in excluding the presence of cancer and its limited specificity in ruling in prostate cancer, due to elevations seen in benign prostatic hypertrophy, prostatitis, and after procedures such as rectal examination, biopsy, and cystoscopy.

Staging

Survival in prostate cancer is dependent upon the extent of tumor progression beyond the capsule of the prostate at diagnosis. Studies show PSA cannot prospectively distinguish localized cancers from those with extracapsular invasion. PSA levels do not reflect tumor burden and pathological stage accurately due to its poor specificity and the decreased production of PSA by high grade, high volume lesions (3,4).

Diagnosis

Diagnostic testing commonly includes the use of digital rectal examination (DRE), PSA measurement, and transrectal ultrasound (TRUS). There is optimism that when combined with these modalities, PSA may lead to earlier prostate cancer detection, but this early detection has not been shown to improve survival.

As stand-alone diagnostic tools, none of the three modalities has a reliable predictive value when positive. The available evidence does not permit conclusions on the true positive predictive value (PPV) of an abnormal DRE, elevated PSA, and the presence of a hypoechoic lesion by TRUS in detecting cancer due to poor study designs, heterogeneous patient samples, and lack of normative PSA cut-off levels in defining an abnormal (positive) test (5,6). Estimates of sensitivity and specificity are often inaccurately quoted in the literature since they are arbitrarily based on the number of tumors detected by the screening test rather than on biopsy-confirmed tumors.

In addition, detection rates are influenced by the method of prostate biopsy. Some argue that performing multiple systematic biopsies of both lobes with the use of the biopsy gun has contributed more to improved detection compared to the addition of PSA itself (7).

There is also a controversial correlation between ultrasonographic characteristics on TRUS and tissue histology, particularly in small cancers. TRUS improves sensitivity but at the cost of decreasing specificity. Chodak argues that "the ultrasonography will undoubtedly result in the diagnosis of more clinically insignificant tumors than are diagnosed currently because some men with abnormal levels of PSA will undergo either a random biopsy or a biopsy of a minimally significant lesion that may accidentally "hit" small volume tumors. Once this occurs, treatment, although probably unnecessary, will be difficult to withhold" (8). The increased detection and the resulting treatments of clinically insignificant disease may actually cause more deaths than could be expected from the disease itself (9).

The potential physical and psychological harms and their medical costs must be weighed against expected current treatment results. Recent studies have challenged the therapeutic value of aggressive treatment of early cancers which results from prostate cancer screening with PSA. One study found that prostatectomy is unlikely to improve survival in patients with locally confined tumors (10), while another concluded that long-term outcomes compare favorably in patients with local cancers treated conservatively versus aggressively (11). Prostate cancer can have a long, stable course without treatment, and understanding its natural history will require long-term, prospective studies.

Treatment Decision

In order to benefit patients with prostate cancer, the PSA test must be highly predictive of the disease and must also result in therapeutic decisions that improve survival. Beyond the indications that we currently cover, a review of the literature does not reveal evidence that knowledge of PSA values, when integrated into the therapeutic decision-making process, alters therapeutic approaches which alter the course of the disease and improve patient outcomes and survival.

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January, 1993

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Antisperm Antibody Test...	WordPerfect document	Thu, Feb 18, 1993, 1:15 PM
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Medical Alley

TECHNOLOGY TASK FORCE REPORT

October 26, 1992

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PREFACE

Minnesota's healthcare delivery system is a world leader in providing high quality care to its patients. Our state is being looked to by Americans and others for answers on how we can continue to provide quality care for individuals while keeping it affordable for our society as a whole. The adoption and use of medical technology is one of the factors which has implications in both of these issues.

With this in mind, Medical Alley -- an organization comprising visionary and energetic leaders from the ranks of the state's healthcare delivery organizations and professionals, medical device manufacturers, research community and payors -- established its **Technology Task Force,** whose membership encompasses all sectors of the healthcare industry.

Medical Alley recognizes that other parties such as employers, consumers, other healthcare professionals and bioethicists have an opinion and stake in medical technology. Their involvement in the Task Force would have made this Report more reflective of a broader societal perspective. The Task Force is, however, comprised of individuals who have specific expertise on the development, assessment, adoption, and use of medical technology. With this expertise, our Report is able to focus on the science and tools surrounding the adoption and use of technology. This necessarily leaves other issues to be discussed, such as values which underlie our healthcare delivery system. We believe these issues merit the deliberation of the broader community.

The Task Force's primary goal was to develop consensus recommendations to ensure the appropriate adoption and use of medical technology. Medical technology is defined by the Task Force as including drugs, devices, procedures, knowledge and/or processes applied to human healthcare. The term appropriate refers to medical technology playing a positive role in enhancing the delivery of effective, quality medical care for patients while mitigating healthcare costs.

This document is intended to serve as a practical framework for decision-making by members of the healthcare industry and others concerned with the implementation of medical technology policy.

TECHNOLOGY TASK FORCE MEMBERSHIP

Chairman, Technology Task Force:
K. James Ehlen, M.D.
Chairman and CEO
MEDICA

H. Clark Adams
VP Business Development
Pharmacia Deltec Inc.

Henry Buchwald, M.D., Ph.D.
Professor of Surgery
U of MN Medical Center

Norman Dann
Partner
Pathfinder Venture Capital

Robert M. Dickler
General Director
U of MN Hospital and Clinic

Robert G. Hauser, M.D.
Chairman and CEO (through 8/92)
Cardiac Pacemakers Inc.

George J. Isham, M.D.
Medical Director
MedCenters Health Plan

John E. Kralewski, Ph.D.
Director Health Services Research
University of Minnesota

Marlene E. Marschall (Ex Officio)
Commissioner of Health
State of Minnesota

Donald V. Murray
Executive Director Industry Relations
3M Health Care

Delwin K. Ohrt, M.D.
VP and Medical Director
Blue Cross Blue Shield of MN

Douglas N. Robinson
Senior Vice President
Fairview Hospitals and
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Lawrence W. Shearon
VP Corporate Technology
Medtronic Inc.

Robert K. Spinner
President
Abbott Northwestern Hospital

James D. Stice
President
Flexmedics Corporation

James V. Toscano
Executive Vice President
Park Nicollet Medical Foundation

Kent S. Wilson, M.D.
Board Representative
Minnesota Medical Association

Staff:
Pamela F. Dinkfelt, Ph.D.
Director Technology Policy
Medical Alley

INTRODUCTION

Medical technology contributes substantially to the health and well-being of the patient. In fact, improvement of the health status of the patient is the primary motivation behind the development of new medical procedures and products. However, technology's responsible and appropriate use is one of the issues under scrutiny as society searches for ways to slow the upward spiral of healthcare costs and improve access to affordable healthcare among the uninsured and underinsured.

Healthcare spending in the United States has increased from $280 billion in 1980 to an estimated $817 billion in 1992. This growth exceeds the rate of inflation and now consumes approximately 13 percent of the GNP, up from 9 percent in 1980. With medical technology defined as including drugs, devices, procedures, knowledge, and/or processes, the intensive use of these technologies is estimated to account for 20 to 40 percent of overall healthcare spending. Technology's impact on overall healthcare costs is complex. Medical technology can be, and most often is, used appropriately -- that is, to enhance the delivery of high quality care while also helping to hold down cost increases.

Our society, however, has had a long-standing fascination with innovation. At times, healthcare spending has been fueled by an insatiable demand for the newest and latest in technology without full knowledge of a technology's cost or its overall ability to improve patients' health outcomes. In some cases, technologies have been purchased for their potential to improve patient market share. In competing for patients, sometimes the latest technologies are purchased and then overused to keep current with the perceived community standard.

Unrealistic expectations on the part of patients and the ever-present threat of litigation have lead some physicians to resolve diagnostic and treatment quandaries by more extensive procedures and testing than may be required. Patients may demand the use of technologies based on premature, over-optimistic media reports comforted by the knowledge that they are shielded from most of the costs by employer- and taxpayer-subsidized insurance. Historically, technologies have been reimbursed independent of results, and use of these technologies have sometimes been ineffective or unnecessary.

On the other hand, appropriately used newer technologies expose patients to generally less risk and achieve better outcomes than those used in the the past. For example, uncomfortable diagnostic procedures performed on the central nervous system have been replaced by noninvasive imaging techniques which provide more information of higher accuracy. Technology has also reduced the surgical recovery time; for instance, laparoscopic cholecystectomy, a procedure for removing the gallbladder. Traditional gallbladder surgery requires a large incision and a two- to six-week recovery time; laparoscopy allows physicians using fiberoptic technology to perform the surgery through small incisions with minimal hospitalization and a recovery time of a few days.

Advances in technology have made it possible to provide patient care in less expensive settings; many eye and musculoskeletal procedures can now be performed without hospitalization, and portable infusion pumps enable chemotherapy treatment to take place at home. Medical technology has enhanced the lives of patients by reducing pain and increasing mobility, and has enabled patients to stay in their own homes rather than nursing homes. Advanced technologies, such as coronary angioplasty and cardiac pacemakers, enable patients to now return to work in days rather than weeks, reducing sick leave and adding to, rather than taking from, the community tax base.

The dramatic changes in the delivery of healthcare and rising healthcare costs require that more informed choices be made regarding medical technologies. How and when technology is used must be examined, and misuse eliminated. The use of technologies without thorough knowledge of efficacy is costly, especially when total healthcare resources are limited.

This report is intended to guide more informed decisions about medical technology while nurturing and enhancing the environment for healthcare innovation.

EXECUTIVE SUMMARY

TECHNOLOGY TASK FORCE GOAL:

The primary goal of the Technology Task Force has been to develop a series of consensus recommendations to ensure the **appropriate** use of medical technology.

- Medical technology is defined as including drugs, devices, procedures, knowledge, and/or processes applied to human healthcare.
- The term *appropriate* refers to technology enhancing the delivery of effective, quality medical care for patients while at the same time mitigating healthcare costs.

INTENT:

The Technology Task Force intends for its recommendations to serve as a framework for those interested in healthcare reform and addressing issues related to the appropriate adoption and use of technology. The recommendations are not an absolute standard, but a tool to be used in conjunction with professional interpretation when applied to specific decisions about technology.

The Report seeks to:

- Delineate the questions that need to be asked of those who develop, provide, pay for, or receive technologies, and
- Facilitate the responsible diffusion of technology from the research environment to the general medical community.

The Task Force hopes that the recommendations herein will stimulate discussion among members of the healthcare industry, private and public policymakers at the regional, state, and national levels, and other parties interested in the implementation of medical technology policy.

OVERVIEW:

This Report is significant because it represents the work of an industry-wide task force, unique in its composition, which dedicated itself to move beyond self-interest, collaborate, and respond to society's concern regarding availability of technology for patients and rising healthcare costs.

In considering the recommendations in this Report, it is important to remember the following:

- The climate for technology innovation is fragile due to the high costs of research and development, reduction of research funding, and regulatory restrictions.
- The Task Force sought to create a process for patients to have ready access to beneficial, innovative technologies while ensuring that the technologies are safe and cost effective.
- The Task Force recognized, however, that technology assessment is a relatively new strategy in healthcare evaluation and is not yet a completely scientific endeavor. The number of new and existing technologies to be assessed far outstrip the available trained personnel and financial resources. The process of technology assessment, as pertinent and valuable as it is, should not inadvertently serve to inhibit patients access to beneficial care.
- The Task Force makes its recommendations, therefore, asking that prudent consideration be used in their application.

The Technology Task Force Report encompasses four dominant themes:

- **Principles**
- **Technology phases**
- **Standardized criteria**
- **Further necessary action**

Principles:

The Task Force recommendations are developed based on principles related to preserving and nurturing technology innovation while providing guidance as to how to ensure appropriate adoption and use of technology.

Technology phases:

The recommendations address the medical technology process across a continuum, including the research, development, application, and financing phases of technology innovation.

Standardized criteria:

The recommendations present criteria for the:

- Prioritization of which technologies should undergo assessment;
- Assessment of technology safety, clinical effectiveness, ability to improve patients' health outcome, and cost effectiveness;
- Providers' use of technology; and
- Development of practice parameters.

These criteria are generic and applicable across the phases of development and application of technology by researchers, manufacturers, providers, payors, and regulators. The criteria have been compiled to create a common language to facilitate communication and responsible decision-making among all those concerned with technology.

Further necessary action:

The Task Force makes a call for community action to develop private and public policies that address societal and ethical concerns including patient expectations, and legal reform in the areas of antitrust and liability. While the recommendations create a framework to ensure appropriate adoption and use of technology, these other issues could significantly affect whether or not the implementation of the recommendations can come to fruition, and these issues merit deliberation from the broader societal perspective.

PRINCIPLES

The recommendations of the Technology Task Force were developed based on principles related to preserving and nurturing technology innovation while providing guidance as to how to ensure appropriate adoption and use of technology.

The Task Forces believes that:

- The focus of technology assessment is to ensure appropriate adoption and use of technology.
- A priority-setting process is to be used by all concerned parties to determine which technologies should undergo assessment.
- Standardized technology assessment criteria are to be agreed upon and used across the healthcare industry by scientists/researchers, manufacturers, providers, and payors.
- Responsible judgment is central to the use of technology assessment criteria.
- Technologies are to demonstrate safety, clinical effectiveness, ability to improve health outcomes, and cost effectiveness prior to their widespread diffusion into the medical community.
- Third-party payors are to consider provisional coverage of technologies undergoing scientifically sound clinical trials.
- Medical product manufacturers, healthcare delivery organizations and professionals, and payors -- among themselves and between groups -- are to develop collaborative relationships for the conduct of research.

TASK FORCE RECOMMENDATIONS

Technology Assessment:

- A medical technology should undergo assessment to determine its safety, clinical effectiveness, ability to improve patients' health outcome, and cost effectiveness.
- A priority-setting process should be used by all concerned parties to determine which technologies should undergo assessment.
- Standardized technology assessment criteria should be agreed upon and used across the healthcare industry by scientists/researchers, manufacturers, providers, and payors.
- Technology assessment should be an iterative process with technologies reevaluated on an ongoing basis.

Technology Diffusion:

- The pace and the extent to which a technology diffuses into the medical community should be dependent on the technology's level of demonstrable safety, clinical effectiveness, ability to improve patients' health outcome, and cost effectiveness.

Provider Use of Technology:

- Providers should meet standards criteria for the use of a given technology.
- Centers/institutes should exist for patients who have a condition associated with significant mortality and/or morbidity requiring both a high level of professional expertise and technologic resources to treat (e.g., bone marrow transplant for leukemia), or for technologies that represent a high-cost expenditure (e.g., magnetic resonance imager).
- Rather than a priori establishing a given number of centers for high-patient-risk or high-cost technologies, centers should meet established standards criteria.
- The use of the nomenclature, "centers of excellence", by the healthcare industry should be abandoned.

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TASK FORCE RECOMMENDATIONS (continued)

Practice parameters:

- Practice parameters should be developed to guide patient management in relation to the use of medical technology.

Intraindustry research collaboration:

- Third-party payors should consider provisional coverage of technologies undergoing scientifically rigorous clinical trials.
- Medical product manufacturers, healthcare delivery organizations and professionals, and payors -- among themselves and between groups -- should develop collaborative relationships for the conduct of research.

Technology knowledge:

- Well documented, accurate information on technologies should be communicated to providers of patient care, and findings actively integrated into research and clinical practice.
- The healthcare industry should provide technology information to patients.
- A clearinghouse should exist for technology-related information.

Further action:

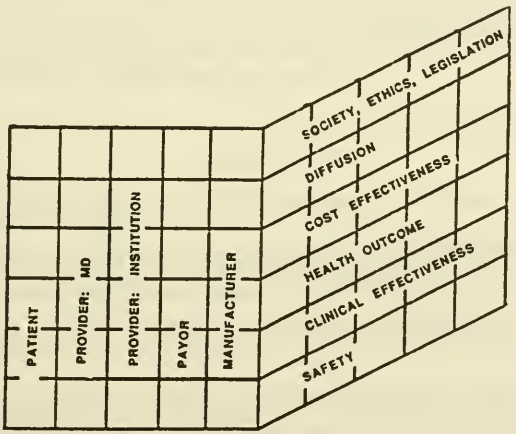
- There are issues that could affect whether or not the implementation of the Task Force recommendations can come to fruition. These issues include:
  - Societal and ethical concerns relative to patient expectations, and quantity and quality of life.
  - Support for ongoing education and training of scientists and clinicians.
  - Legal reform in the areas of antitrust and liability.

APPROPRIATE ADOPTION AND USE OF TECHNOLOGY

As the figure below depicts, in order for a technology to be appropriately adopted and used, it must be safe, clinically effective, able to improve patients' health outcomes, and cost effective. Appropriate use also includes the dynamics of technology diffusion (the when, how, and by whom technology is used). These components are highly interdependent, impact on one another, and will be the focus of the Task Force recommendations. In addition societal, ethical, and legal factors impact on technology use and need to be taken into consideration.

The components of appropriate adoption and use of technology will be addressed in this Report from the perspective of the patient, provider, payor and manufacturer. (Appendix A illustrates the intraindustry process of medical technology development and diffusion.)

INTERDEPENDENCE OF TECHNOLOGY COMPONENTS AND PATIENTS - PROVIDERS - PAYORS - MANUFACTURERS



TECHNOLOGY ASSESSMENT

A medical technology should undergo assessment to determine its safety, clinical effectiveness, ability to improve patients' health outcome, and cost effectiveness.

Dramatic changes in the delivery of healthcare and rising healthcare costs call for more informed choices about medical technologies. Technology assessment refers to the systematic process of evaluating properties of a medical technology including such factors as its safety, clinical effectiveness, ability to improve patients' health outcome, and cost effectiveness. The prudent use of technology assessment can act as a cogent bridge between the research and development of a technology and its appropriate use in our medical community.

Traditionally, technologies have tended to move from the research environment into general medical practice without an orderly assessment process. Faced with the immediacy of a sick patient and a remote possibility that a new intervention may prove beneficial, it is the rare patient, family, or physician who do not want to act. As a result, an innovation that makes theoretical sense sometimes becomes established practice before it is determined that it can make a significant difference in a patient's health outcome. Using a technology without established benefit could expose a patient to an unnecessary health risk and possibly keep the patient from undergoing an alternative treatment that could provide benefit. The technology assessment process can expedite the expanded use of technologies with demonstrable benefits and the early abandonment of those with minimal benefit.

The systematic assessment of patients' health outcomes and costs related to the use of technologies can yield a foundation for both clinical decision-making and constructive public policy formulation. Knowing the extent to which a technology can provide a cost-effective advantage over alternative technologies can serve to enhance the quality of healthcare we deliver, maximize the efficiency of our healthcare system, and optimize healthcare expenditures.

TABLE 1

DEFINITIONS

Safety refers to the acceptability of risk in using a technology or the technology's potential for causing harm.

Clinical effectiveness incorporates safety, and refers to the technology improving patients' clinical status (i.e., morbidity, mortality) and to the use of this particular technology demonstrating a clinical advantage over alternative technologies.

Health outcomes is a global term incorporating safety, clinical effectiveness, and quality-of-life issues such as life satisfaction, ability to function, and ability to return to work.

Cost effectiveness refers to the costs of using a particular technology to achieve improvement in a patient's health outcome compared to both the costs and the extent of improvement in patient health outcome resulting from the use of alternative technologies.

Diffusion refers to the movement of technology use from the research and development environment into general medical community application.

A priority-setting process should be used by all concerned parties to determine which technologies should undergo assessment.

Technology assessment is an important, but relatively new strategy in healthcare evaluation. The number of new and existing technologies to be assessed far outstrip the available trained personnel and financial resources. The process of technology assessment, as pertinent and valuable as it is, should not inadvertently serve to inhibit patients' access to such care.

A priority-setting process can best determine which technologies should undergo assessment. There are different types of technology with varied levels of health and economic importance, as well as other issues of importance which may have assessment significance. **Professional judgment and common sense must prevail in determining which technologies should be assessed.** A conscious balance must exist between patients' access to beneficial care with the time required for extensive technology evaluation.

Table 2 displays the criteria which can serve as a guide to help identify technologies which an assessment can have the greatest impact. Use of prioritization criteria could provide patients with greater access to beneficial technologies and avoid the expense of unnecessary evaluation.

TABLE 2

PRIORITIZATION CRITERIA FOR TECHNOLOGY ASSESSMENT

IN PRIORITIZING TECHNOLOGIES TO UNDERGO ASSESSMENT, THE FOLLOWING POINTS SHOULD BE CONSIDERED:

- Negative/positive impact on patient safety and health outcome; public health importance (e.g., HIV therapies).
- Economic implications: large initial capital expense, large cumulative operating expense, major cost-savings or cost-inducing (e.g., mobile angiography).
- Rapid diffusion (e.g., laparoscopic cholecystectomy).
- Impact on a substantial patient population (e.g., treatment for hypertension).
- Controversy within medical or scientific community; gap between current knowledge and practice (e.g., autologous bone marrow transplant for breast cancer).
- Existence of alternative technologies (e.g., TPA versus Streptokinase).
- Level of public/professional demand for the technology (e.g., prostate specific antigen).
- Social, ethical or legal concern (e.g., end-of-life care).
- Rare diseases/conditions (e.g., Ceredase for Gaucher's disease).

Standardized technology assessment criteria should be agreed to and used across the healthcare industry by scientists/researchers, manufacturers, providers, and payors.

The different sectors of the healthcare industry currently use varied criteria to assess technology. With the large number of innovative technologies emerging from scientific research and limited healthcare resources, it is imperative that we adopt more systematic mechanisms. Standardized assessment criteria will enhance efficient review of medical technologies by having those producing data on technology (e.g., researchers, manufacturers) and those reviewing that data (e.g., providers, payors) consistently knowing the nature of assessment information that will be required. Obviating assessment redundancy will expedite the use of beneficial technologies and lower healthcare costs.

The Task Force recommends the standardized criteria described in Tables 3 and 4.* When feasible, technology assessment ought to be undertaken for patients' health outcomes and cost effectiveness concurrently to facilitate timely evaluation.

Assessment of a technology should take into consideration an entire episode of care, including immediate results of using the technology and its long-term impact on health outcome and costs for the patient and the patient's community. The primary objective in technology assessment is the development of accurate information on medical technology, and as described in the criteria, this information must be based on scientifically sound data.

*The Task Force recognizes, however, there are variations in both the methods and outcomes of technology assessment. Technology assessment today isn't a single process. The types of assessment can range from a simple search of the literature to a more comprehensive method such as the collection of new data in the form of randomized clinical trials. Assessments performed by a variety of entities ensure a balancing mechnism in an area where medical and technical judgment can vary widely. A variety of assessors avoids the risk of an erroneous or premature decision which could preclude important medical advances for patients.

TABLE 3

ASSESSMENT CRITERIA

SAFETY - CLINICAL EFFECTIVENESS - HEALTH OUTCOME

The five technology assessment criteria described below will serve as a guide to determine whether a medical technology demonstrates **safety, clinical effectiveness,** and improvement in patients' **health outcomes***.

Safety refers to the technology's potential for causing harm. **Clinical effectiveness** incorporates safety, and refers to the technology improving patients' clinical status (i.e., mortality, morbidity) and to the use of this particular technology demonstrating a clinical advantage over alternative technologies. **Health outcomes** incorporates safety, clinical effectiveness, and quality-of-life factors such as life satisfaction, ability to function, and ability to return to work.

Assessment of the technology should be global in perspective, taking into consideration an entire episode of care, including the immediate results and the long-term impact for the patient and the patient's community.

All five criteria should be met, with technology **safety** being central to each criterion and to the determination of a technology's impact on net health outcome.

Responsible judgment (professional common sense) is to be applied in using these criteria to assess a technology and indications for its use.

- **IF APPLICABLE, THE TECHNOLOGY SHOULD HAVE FINAL APPROVAL FROM THE APPROPRIATE GOVERNMENT REGULATORY BODIES.**

  If applicable, a technology should have Food and Drug Administration (FDA) approval to market for those specific indications and methods of use that are being assessed.

  Approval to market refers to permission for commercial distribution. Any other approval that is granted as an interim step in the FDA regulatory process (e.g., Investigational Device Exemption) would not be sufficient. (Refer to Appendix B for a description of the FDA process.)

- **THE SCIENTIFIC EVIDENCE SHOULD PERMIT CONCLUSIONS CONCERNING THE EFFECT OF THE TECHNOLOGY ON HEALTH OUTCOMES****.

  The evidence should consist of well-designed and well-conducted investigations, preferably published in peer-reviewed journals. The scientific rigor of the body of studies and the consistency of the results are considered in evaluating the evidence.

  The evidence should demonstrate that the technology can measure or alter the physiological changes related to a disease, injury, illness, or condition. In addition, there should be evidence or a convincing argument based on established medical facts that such measurement or alteration affects patient health outcomes.

  Opinions and assessments by national medical associations, consensus panels or other technology assessment bodies are evaluated according to the scientific quality of the supporting evidence and rationale.

(CONTINUE ON NEXT PAGE)

TABLE 3 (CONTINUED)

ASSESSMENT CRITERIA

SAFETY - CLINICAL EFFECTIVENESS - HEALTH OUTCOME
(CONTINUED)

- **THE TECHNOLOGY SHOULD IMPROVE NET HEALTH OUTCOME.**

  The technology's beneficial effects on health outcomes should outweigh the risk of harmful effects on health outcomes [e.g., automatic implantable cardiac defibrillator (AICD)].

- **THE TECHNOLOGY SHOULD IMPROVE NET HEALTH OUTCOME AS MUCH AS, OR MORE THAN, ESTABLISHED ALTERNATIVES.**

  The technology should be at least as beneficial as any established alternatives (e.g., AICD versus drug therapy).

- **THE IMPROVEMENT IN NET HEALTH OUTCOME SHOULD BE ATTAINABLE OUTSIDE THE RESEARCH ENVIRONMENT.**

  When used under the usual conditions of medical practice, the technology should be reasonably expected to satisfy the listed third and fourth criteria.

* Criteria adapted from that used by the Blue Cross and Blue Shield Association.
** For brevity the terminology health outcome will include safety and clinical effectiveness.

TABLE 4

ASSESSMENT CRITERIA

COST EFFECTIVENESS

The technology assessment criteria described below will serve as a guide to determine whether a medical technology demonstrates **cost effectiveness**. When feasible, there should be concurrent assessment of patients' health outcomes and cost effectiveness.

Cost effectiveness refers to the costs of using a particular technology to achieve improvement in a patient's health outcome compared to both the costs and the extent of improvement in patient health outcome resulting from the use of alternative technologies. For example, a cost effective technology would be one in which the patient's ability to return to work sooner and the concomitant employer/employee economic and societal benefits justify the costs related to the use of the particular technology over an alternative technology.

Assessment of the technology should be global in perspective, taking into consideration an entire episode of care, including the immediate results and the long-term impact for the patient and the patient's community.

Responsible judgment (professional common sense) is to be applied in using these criteria to assess a technology and indications for its use.

A TECHNOLOGY WILL MEET COST-EFFECTIVENESS CRITERIA IF IT IS:

- At least as effective and less costly than alternative technologies, or
- More effective and more costly than alternative technologies, but resultant patient health outcomes justify additional expenditures, or
- Less effective and less costly than alternative technologies, but resultant patient health outcomes from use of alternative does not justify additional expenditures.

	IMPROVED HEALTH OUTCOME*		
COSTS	MORE	SAME	LESS
MORE	Dependent on Outcomes/Cost	Not Cost Effective	Not Cost Effective
SAME	Cost Effective	Dependent on Outcomes/Cost	Not Cost Effective
LESS	Cost Effective	Cost Effective	Dependent on Outcomes/Cost

[In the assessment of cost effectiveness, factors related to patient health outcomes are quantified (e.g., patient was able to return to work in eight days versus one month). When feasible, cost benefit analysis should be used; in the assessment of cost benefit, factors related to patient health outcomes are examined in monetary terms (e.g., dollars saved by having the patient return to work in the eight days).]

* Table adapted from Deber, 1992.

Technology assessment should be an iterative process with technologies reevaluated on an ongoing basis.

Assessment of medical technology should be an iterative process, not a single event; particularly if the technology is expensive or has the potential to cause patient harm if used incorrectly. To be workable, technology assessment should be flexible, allowing for ongoing clinical input and periodic review as new data become available. Given time, outcome studies may show that the technology is not as safe as it was originally thought. Even a seemingly tried-and-true technology, when compared to its successor and competing technologies, may become obsolete or only marginally useful.

The continued use of obsolete technologies adds to the costs of providing healthcare to patients. By reducing this activity, the use of more cost effective technologies that contribute to the improvement of patients' health outcomes could be facilitated into the mainstream of medicine.

TECHNOLOGY DIFFUSION

The pace and extent to which a technology diffuses into the medical community should be dependent on the technology's level of demonstrable safety, clinical effectiveness, ability to improve patients' health outcome, and cost effectiveness.

Diffusion refers to the use of technology; it is the movement of technology use from the research and development environment into general medical community application.

In order to ensure appropriate use of technology, the pace and extent to which a technology diffuses into the medical community should be dependent on the technology's level of demonstrable safety, clinical effectiveness, ability to improve patients' health outcome, and cost effectiveness.

Table 5 shows that technologies that are undergoing clinical research trials to determine these factors should have only **limited diffusion**. The technology should be retained in the research and development environment and not be used in the general medical community. An example of such a technology would be in vitro gene manipulation.

In **expanded diffusion**, the technology is beyond the stage of clinical trials, is used by some providers beyond the research and development environment, but is not in widespread use in the general medical community. A technology with expanded diffusion should have already demonstrated safety, clinical effectiveness, and ability to improve patients' health outcome. It should not have widespread diffusion, however, because it needs further cost-effectiveness analyses and/or patient outcome studies, or is associated with high-patient-risk or high-cost (e.g., bone marrow transplant).

With **widespread diffusion**, the technology has demonstrated safety, clinical effectiveness, improvement in patients' health outcomes, and cost effectiveness and is used across the general medical community (e.g., gynecologic fiberoptic technology).

(Appendix A illustrates the intraindustry process of medical technology development and diffusion.)

TABLE 5

TECHNOLOGY DIFFUSION SUMMARY

LIMITED DIFFUSION

The technology is retained in the research and development environment, and is not in use in the general medical community. The given technology would be undergoing clinical research trials to determine safety, clinical effectiveness, and ability to improve patients' health outcome in relation to a given clinical indication by providers that meet minimum standards criteria for the safe and beneficial use of the technology in relation to patient volume, personnel, facilities, outcome success rates, outcome management, data reporting, research, and education. If feasible, cost effectiveness analysis should be conducted.

↓

EXPANDED DIFFUSION

The technology is beyond the stage of clinical trials, but is not in widespread use in the medical community. The given technology would have demonstrated safety, clinical effectiveness, and ability to improve patients' health outcome in relation to a clinical indication but the technology needs further cost-effectiveness analysis and/or outcome studies, or the technology is associated with high-patient-risk or high-cost. Technology would be used by those providers that meet minimum standards criteria for the safe and beneficial use of this technology in relation to patient volume, personnel, facilities, outcome success rates, outcome management, data reporting, research, and education.

↓ ↓

WIDESPREAD DIFFUSION

Technology would be diffused into widespread use in the medical community. The given technology would have demonstrated safety, clinical effectiveness, ability to improve patients' health outcome, and cost effectiveness in relation to a clinical indication, and would be used by those providers that meet minimum standards criteria for the safe and beneficial use of this technology in relation to patient volume, personnel, facilities, outcome success rates, outcome management, data reporting, research, and education.

USE OF TECHNOLOGY

Providers should meet standards criteria for the use of a medical technology.

A medical technology is not an isolated entity; it is used by human hands in a healthcare environment. As Table 5 shows, the pace and extent to which a technology is diffused should also be dependent on providers' ability to meet standards criteria for the use of the technology.

To ensure quality, effective delivery of care, Table 6 lists standards criteria that can serve as a guide for providers offering medical technologies To ensure quality, effective delivery of care. National and regional specialty groups should be looked to for specific criteria for a given technology as it relates to personnel, facilities, patient volumes, patient health outcomes, data reporting, research, education, and patient involvement. The table also lists criteria related to patient access to care, community cost effectiveness, and financial support.

The criteria delineate a series of points that providers may need to take into consideration when using technologies. For example, the criteria make mention of research. With IV placement, little would be required in terms of research; the study of a more specialized technology, such as cardiac pacemakers, would require more extensive facilities and professionals to enable the conduct of research. In taking this point into consideration, a provider may be able to address it by having access to professionals via computer modem.

The extent to which a provider needs to address these standards criteria depends on the type of technology. By example, the placement of an IV line requires much less in terms of personnel, facilities, and data reporting than the placement of a cardiac pacemaker.

TABLE 6

PROVIDER STANDARDS CRITERIA

MINIMUM STANDARDS CRITERIA:

National and regional specialty groups should be looked to for the specific criteria necessary for the safe and beneficial use of a given technology for a particular clinical indication. Depending on the type of technology, minimum standards requirements may be established for:

- **Personnel:** Sufficient number of professionals and ancillary staff committed to involvement with the particular technology/clinical indication. These individuals must be able to document that they have the necessary knowledge, training, and experience. Comparable requirements need to be met by medical/surgical/radiological support specialties.
- **Facilities:** Sufficient facilities and equipment, and support facilities and equipment, for use of the given technology and management of patients.
- **Patient volume:** Sufficient number of patients treated per given time period to ensure ongoing expertise.
- **Patient health outcomes:** Satisfactory success rates.
- **Patient health outcome management:** Patient outcome data collected and deficiencies identified on a continuing basis for analyzing causes, and for implementing changes directed at improving patient outcomes.
- **Data reporting:** Outcome data reported to national and regional registries (e.g., National Cancer Institute, Minnesota Health Care Commission), and findings published in the scientific/medical literature.
- **Research:** Sufficient facilities and number of professionals with documented biostatistical/research design knowledge, training, and experience to enable research.
- **Education:** Sufficient facilities and personnel to enable clinical education and training.
- **Patient/family involvement:** Sufficient programs in place to inform patients and their family of benefits, risk, and cost of technology, and to involve them in medical decision making.

ADDITIONAL CRITERIA:

These criteria may also need to be met:

- **Access:** Provider/payor provisions made for access to technology for patients in rural areas and those who are unable to pay.
- **Community cost effectiveness:** Clinical patient need exists in sufficient numbers in the provider's community service area to demonstrate cost effective use of technology.
- **Financial support:** Demonstrable financial reserves available to provide ongoing support for the technology.

Centers/institutes should exist for patients who have a condition associated with significant mortality and/or morbidity requiring both a high level of professional expertise and technologic resources to treat (e.g., bone marrow transplant for leukemia, heart transplant), or for technologies that represent a high-cost expenditure (e.g., magnetic resonance imager).

Rather than a priori establishing a given number of centers for these high-patient-risk technologies or high-cost technologies, centers should meet established standards criteria.

Improved health outcomes and cost effectiveness of patient care would be optimized by having centers exist for high-patient-risk or high-cost technologies by the coordination and possibly the centralization of professional expertise and facilities.

The number of such centers should not be established a priori. Rather, providers should demonstrate their ability to meet standards criteria relative to patient volume, personnel, facilities, patient health outcomes, patient health outcome management, data reporting, research, and education (Table 6). The high level of professional knowledge and training necessary, and the patient volume required to ensure ongoing expertise, will in itself become self-limiting factors.

The use of the nomenclature, "centers of excellence", by the healthcare industry should be abandoned.

The healthcare industry should abandon the use of the "centers-of-excellence" nomenclature. The term is imprecise and has marketing implications that can be misleading to the public. All healthcare delivery centers should strive for excellence; the establishment of centers of excellence by definition could be thought to establish centers of nonexcellence.

PRACTICE PARAMETERS

Practice parameters should be developed to guide patient management in relation to the use of medical technologies.

Practice parameters are patient management strategies that assist physicians in clinical decision-making. These systematically developed statements delineate appropriate technology use in specific clinical circumstances and can guide the allocation of healthcare resources.

By example, when medical or scientific evidence is equivocal or inconclusive, practice parameters can assist the physician in selecting technologies most likely, based on current knowledge, to produce significant improvement in patients' health outcomes. When equally effective technologies exist, practice parameters can define a range of acceptable strategies given patient characteristics, desired health outcomes, and technology cost effectiveness.

Practice parameters should be developed by or in conjunction with physician and other healthcare professional organizations (see Table 7). These organizations have the expertise and broad-based representation necessary to develop scientifically and clinically sound practice parameters which will be accepted and used by physicians in their day-to-day practice of medicine. Due to the great variability in medical information, development of parameters should include the documentation and synthesis of relevant scientific studies, research findings, clinical experience, and expert opinion. This medical information should be current, and given the fast pace of innovation, practice parameters should be written with provisions for periodic reviews. Emergence of new technologies should be monitored, and those technologies that show evidence of improving patients' health outcomes should be brought to the attention of organizations that develop parameters.

To enhance the integration of parameters among physicians, parameters should describe indications for technology use in specific clinical situations. This approach would enable physicians to implement and evaluate patient outcomes more systematically. Allowance, however, should be made for variation in care due to individual circumstances. These variations should be subjected to periodic analysis for the refinement of parameters.

Traditionally, physician organizations have not used cost as a factor in the formulation of practice parameters. Although physicians' primary concern should, and must be, the delineation of management strategies that promote patients' improved health outcomes, physicians must also address the economic costs of achieving that outcome. When cost effectiveness is incorporated into the development of a practice parameter, it should be clearly documented.

TABLE 7

CRITERIA TO GUIDE PRACTICE PARAMETER DEVELOPMENT

PRACTICE PARAMETERS SHOULD BE:

- Developed by or in conjunction with physician and other healthcare professional organizations;
- Based on reliable methodologies that integrate relevant research findings and clinical expertise;
- Based on current information;
- As specific as possible; and
- Widely disseminated.

THESE PARAMETERS SHOULD:

- Include statements describing the critical facts on which parameters were based (e.g., scientific literature, cost-effectiveness analysis);
- Be defensible in light of current scientific evidence;
- Emerge from an open, fair, and credible process;
- Be described in a fashion that expedites implementation by practitioners.
- Include allowance for variation due to individual patient circumstances.
- Automatic sunset on a time schedule that forces regular review.

*Criteria adapted from that used by the American Medical Association.

INTRAINDUSTRY RESEARCH COLLABORATION

Third-party payors should consider provisional coverage of technologies undergoing scientifically rigorous clinical trials:

When a patient is enrolled in a clinical trial of a particular technology, the patient's third-party payor should consider reimbursing for the studied technology at a predetermined, negotiated reimbursement level after the following conditions are weighed:

- **Scientific rigor of the research protocol,**
- **Institutional review board (IRB) approval,**
- **Professional expertise of the clinical and research personnel, and**
- **Potential benefit for the patient.**

The search for more effective ways to prevent, diagnose, and treat disease is acutely sensitive to regulatory and reimbursement policies that influence the progression of technologies from the investigational stage into the clinical arena. These policies should be delicately balanced to assure the safety and effectiveness of the technology while facilitating their movement into clinical medicine.

Data obtained from clinical trials are a crucial component of the technology assessment process. The National Institutes of Health and other funding agencies, however, are limiting funding for clinical research for University and non-University providers, as well as for manufacturers. In addition, smaller/newer companies lack resources to conduct extensive clinical trials.

Policymakers in the public and private sectors sometimes find it difficult to specify when a new technology ceases to be investigational (generally not reimbursed by payors) and when it becomes accepted practice in the medical community (generally reimbursed). Providing payment for promising investigational technologies undergoing well-designed and well-conducted clinical trials would enhance patients' opportunity to have access to promising therapy, and also enhance the likelihood that sufficient numbers of patients could be recruited to enable studies to be completed in a more timely fashion.

Payors may also consider pursuing a formal distinction for "provisional technologies" as a nomenclature used for promising technologies that are receiving temporary/limited reimbursement while undergoing specified clinical trials. This terminology may be helpful in both the legal and regulatory realms.

Medical product manufacturers, healthcare delivery organizations and professionals, and payors -- among themselves and between groups -- should develop collaborative relationships for the conduct of research.

Joint provider and/or payor participation in clinical trials would expedite availability of potentially beneficial technologies for patients. The healthcare industry would have an enhanced scientific data base enabling it to make sound decisions relative to technology safety, clinical effectiveness, improvement in health outcome, and cost effectiveness.

TECHNOLOGY KNOWLEDGE

Well-documented, accurate information on technologies should be communicated to providers of patient care and information actively integrated into clinical practice.

A major reason for conducting healthcare research -- clinical trials, outcome studies, technology assessment, or practice parameters -- is to improve the delivery of effective, quality care for patients. Those who conduct healthcare research have a responsibility to communicate findings from their work in an accurate, timely manner. These findings need to be reproducible, thus need to be based on well-designed and well-conducted studies that represent scientific rigor.

These research findings must get into the hands of physicians and others who can use them constructively. There is general support for the development of better information as a means to better healthcare, a key question remains as to how to ensure that the information is received, interpreted, and used properly. Physicians are faced with an enormous, ever-expanding volume of scientific literature and research findings, much of which may not be relevant to their clinical practice or is in conflict with other research findings.

Healthcare research projects need to include protocols delineating their plan for sharing and integrating results. Organizations developing healthcare-related data must be cognizant that excessive distribution exacerbates information overload. The data need to be synthesized into readily accessible, understandable monographs dealing with specific issues. User-friendly decision aids (e.g., computer programs) that relate information about specific types of patients to research findings deserve special emphasis.

The healthcare industry should provide technology information to patients.

Patients are no longer passive recipients of medical care; indeed, they have a right to information regarding benefits, risks, and costs of the medical technology used in their care. Given the structure of third-party reimbursement, patients often are not aware of the cost of technology. By empowering patients and their families with accurate technology information, they are able to actively participate in medical decisions and form more realistic expectations about probable short- and long-term outcomes. In doing so, patients can become part of the solution of mitigating healthcare spending.

A clearinghouse should exist for technology related information.

A resource should exist to track information on medical technology for the healthcare industry and the public. Medical practitioners and patients alike should have access to a clearinghouse of accurate data about benefits, risks, and options related to specific medical conditions and their related costs.

FURTHER ACTION

FURTHER ACTION

The Technology Task Force was comprised of those who had specific expertise in the development, assessment, adoption, and use of medical technology. The Task Force recognized, however, that there are a variety of other parties with an opinion and stake in the adoption and use of medical technology such as employers, consumers, other healthcare professionals, legal/legislative professionals, and bioethicists. While the Task Force's recommendations create a framework to ensure appropriate adoption and use of technology, there are issues that could significantly affect whether or not the implementation of these recommendation can come to fruition, and these issues merit deliberation from the broader societal perspective. Healthcare is a community resource, and the Task Force calls for community action.

Quantity and Quality of Life, Patient Expectations

We need to become more cognizant of community and personal values as it relates to medical technology. In particular, we need to learn about patients' and families' concerns relative to technology and incorporate their requests relative to issues such as quantity and quality of life. At the same time, there is a need for our community to become more realistic as to what can be actually achieved by medical technology. In the past, healthcare has been sold as a free good in our economic system. There has been a perception that if a person becomes sick everything will be done and there will be no need to be concerned about costs. Hard decisions need to be made now as to the extent of care that should be received when the outcome of the care is uncertain, and the societal and/or economic cost is high.

Healthcare Education and Research

In order to have our community and its patients be able to make more informed choices on healthcare, we need to support the ongoing education and training of clinicians and scientists to enable further technology innovation and its systematic evaluation. Clinicians and scientists need to be in place, now and in the future, that have the skills to conduct research and produce sound data to base decisions. In this same vein, we need to have closer cooperation within and between the various sectors of the healthcare delivery system. Joint research cooperation would broaden the scientific data base to make decisions.

Legal Reform

Modifications to the antitrust laws are needed to enable intraindustry research collaboration. There is also the need for legal reform of the liability environment for healthcare professionals and medical product manufacturers. Due to the threat of malpractice suits, physicians are sometimes forced to practice "defensive medicine" and order more tests and perform more procedures than truly necessary, and manufacturers are compelled to pursue expensive engineering to ensure that medical products function at a level and length of time not matched by any other group of products. In addition, there is a need to change the regulatory and government process as it relates to payor reimbursement for investigational technologies. Concern has been raised over payor coverage for a specific patient for a promising investigational technology, implying that technology would be covered when demanded by future patients.

INTRAINDUSTRY MEDICAL TECHNOLOGY DEVELOPMENT/DIFFUSION PROCESS

	Bench/Animal Trials	Limited Diffusion	Expanded Diffusion	Widespread Diffusion
MANUFACTURER	• Invention • Concept development • Bench/animal trials	• Product manufacturing • Clinical trials	• Post market studies • Education • Promotion • Sales	• Post market studies • Product improvements • Distribution
FDA	• Review data • Approves clinical trial	• Reviews safety & efficacy • Market approval	• Surveillance	• Surveillance • Policy
PROVIDER/ ACADEMIC INSTITUTIONS	• Concept development • Bench/animal trials	• Feasibility studies • Clinical trial site • Conduct clinical trials • Present/publish findings	• Market research • Purchase decision/installation • Education/training • Credentialing • Provide service • Outcome studies • Cost effective analyses • Present/publish findings	• Provide service • Continuous quality improvement
PROVIDER/ PHYSICIAN	• Concept development • Unmet medical need	• Feasibility studies • Conduct clinical trials • Present/publish findings	• Education/training • Credentialing • Practice parameters • Provide service • Outcome studies • Present/publish findings • Patient education	• Provide service • Continuous quality improvement
PAYOR	• Reimbursement criteria	• Technology assessment • Reimbursement feasibility	• Technology assessment • Reimbursement decision • Outcome studies • Credentialing • Cost effective analyses	• Quality management
PATIENT	• Unmet medical need	• Informed consent • Participate in clinical trial	• Request and/or provided technology • Medical need met (limited) • Education	• Request and/or provided technology • Medical need met • Education

FOOD AND DRUG ADMINISTRATION

The Food and Drug Administration is primarily a scientific regulatory agency for the development of regulations and product standards; development of methodologies and protocols for evaluation of product safety and efficacy; and approval of drugs, medical devices, and other products prior to marketing. Although FDA reviews evidence accumulated in assessments directed by product sponsors, the agency does not conduct clinical trials of medical products. FDA assessment requirements address safety and efficacy but not cost, cost-effectiveness, or broader social issues. Sponsors must show that their products are safe and efficacious as claimed in their labeling, but they are not required to show safety and efficacy relative to similar products.

DRUGS

FDA involvement begins when a sponsor seeks to investigate a drug's safety and efficacy using clinical testing in humans. The FDA has established a two-part process for premarketing drug evaluation; the investigational new drug (IND) application process, and the new drug application (NDA) process.

If the IND application is approved by the FDA, the sponsor may proceed with a three-phase clinical investigation of the drug. Following completion of testing under the approved IND application, a sponsor may file an NDA, which is a request for FDA permission to market the drug.

The agency approves of what the manufacturer may recommend about uses in its labeling and advertising, but it cannot approve or disapprove of how a legally marketed drug is used by a physician in practice. Industry and FDA conduct postmarketing studies of drugs which address some of the needs left unfilled by the premarketing study.

Postmarketing studies include phase IV studies and a variety of surveillance activities. Phase IV studies are not mandated in FDA regulations but are discussed in FDA guidelines. A phase IV study may be a condition of FDA marketing approval if the uncertainty over a drug's safety or efficacy does not warrant delaying its release on the market, or it may be initiated by companies to further substantiate drug safety and efficacy to support marketing efforts.

DEVICES

Device Classification

The Medical Device Amendments of 1976 divided medical devices into three classes -- Class I, Class II, and Class III.

Class I devices are low-risk devices. Examples of devices in this class are enema kits, elastic bandages, and pipetting and diluting systems for clinical use.

Class II devices are medium-risk devices. Examples of devices in this class are hearing aids, catheters, and hard contact lenses.

Class III devices are higher risk devices. Examples include cardiac pacemakers, intraocular lenses, and replacement heart valves.

Product Approval/Clearance Process

A. Premarket Notification [510(k)]

A premarket notification is required from all manufacturers who, after May 28, 1976, introduce: (1) a device into the market for the first time; (2) a device that is substantially equivalent to a device that is already marketed by another manufacturer; (3) a device currently in (or being reintroduced into) commercial distribution that is about to be significantly changed or modified; (4) or a device whose intended use is changed.

Premarket notification, 510(k), is a mechanism through which FDA determines whether the device intended to be entered into commercial distribution is substantially equivalent to a legally marketed device. To be substantially equivalent, the device must have the same intended use as a legally marketed device and either (i) the same technological characteristics as the earlier device, or (ii) different technological characteristics but information demonstrating that the newer device is as safe and effective as the earlier device.

In a 510(k), the FDA reviewer makes an initial determination of whether the device in question performs the same function and is substantially equivalent to a legally marketed device. The review of the premarket notification then compares the characteristics of the device in question (e.g., its design, material, chemical composition, energy source, or manufacturing process) to the characteristics of the legally marketed device. If the differences do not raise new types of safety and effectiveness questions for the same intended use, the device is found to be substantially equivalent and is cleared by FDA for marketing.

It should be noted that in a 510(k) there is no requirement that an actual prototype of a device be manufactured. However, in some cases data from actual device testing are necessary to demonstrate substantial equivalence. These data may be used to demonstrate that the device is equivalent in performance to a preamendment device and/or, if required to provide information about the safety and effectiveness of the device.

If the 510(k) is found not to be substantially equivalent to a legally marketed device, the manufacturer may resubmit another 510(k) with new data, file a reclassification petition, or submit a full premarket approval application (PMA).

The following are exempt from 510(k):

- Devices for commercial distribution not generally available in finished form for purchase, not altered through labeling, or advertising for commercial distribution; and intended for a patient named by order of a physician, or solely for use by a physician, dentist or other professional, and not available to or used by other physicians, dentists or other professional ("custom devices").

- Distributor or repackager selling device under its own name if the labeling and device are not otherwise changed; and the device was in commercial distribution before May 28, 1976 or 510(k) was filed by another.

B. Premarket Approval (PMA)

Most higher risk devices which are not substantially equivalent to a legally marketed device will have to submit a premarket approval (PMA) application prior to marketing. Once the FDA approves a PMA, the device may enter commercial distribution. A PMA is the required process of scientific review to ensure the safety and effectiveness of Class II devices.

The PMA review process consists of: (1) an administrative and limited scientific review by FDA staff to determine completeness ("filing review"); (2) in-depth scientific and regulatory review by appropriate FDA scientific and compliance personnel ("in-depth review"); (3) review and recommendation, if necessary, by the appropriate advisory committee ("panel review"); (4) final deliberation, documentation, and notification of the FDA approval decision. A *Federal Register* notice is published announcing the decision.*

A PMA must contain the information that establishes the safety and effectiveness of the device. In some cases, that information will include the results of clinical trials conducted under an IDE (see below).

*U.S. Department of Health and Human Services, Public Health Service, Food and Drug Administration, *Medical Devices Premarket Approval (PMA) Manual*, October 1986, Reprinted August 1991, HHS Publication, FDA 87-4214.

FOOD AND DRUG ADMINISTRATION

DEVICES (continued)

C. Investigational Device Exemption (IDE)

An IDE is an exemption from certain statutory provisions for devices that are not yet approved for marketing but are being tested in humans to determine safety and effectiveness. The IDE process includes an application filed with FDA, reporting and record-keeping requirements, an appropriate informed consent of patients, and an Institutional Review Board (IRB) review and approval.

An IDE application may be for a significant risk or a nonsignificant risk device. IDEs for significant risk devices must have FDA acceptance and IRB approval. The FDA has 30 days to rule on an IDE submission; and clinical trials may commence after the said period, assuming FDA raises no objections. IDEs for nonsignificant risk devices may commence based solely on an IRB approval.

The *Code of Federal Regulations* (CFR) defines a "significant risk device" as "an investigational device that:

(1) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;

(2) Is purported or represented to be for use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;

(3) Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or

(4) Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject."

All other investigational devices that do not fall under the above "significant risk device" CFR definition are nonsignificant risk devices.

The data gathered during the clinical studies supporting safety and effectiveness are included in a 510(k) and/or PMA submission.

The following are exempt from IDE:

- Devices in commercial distribution prior to May 28, 1976 when used or investigated in accordance with the indications in labeling in effect at that time;
- Substantially equivalent devices when used or investigated in accordance with labeling indications that FDA reviewed in its determination of substantial equivalence;
- Devices undergoing consumer preference testing, testing of a modification, or testing of a combination of devices;
- Devices intended solely for veterinary use of research with laboratory animals; and
- "Custom" devices (except for custom devices when used to determine safety and effectiveness for commercial distribution).

FOOD AND DRUG ADMINISTRATION

DEVICES (continued)

D. Postmarket Controls

Marketed devices are subject to medical device reporting requirements for serious injuries, deaths, and certain types of malfunctions. Under the Safe Medical Devices Act of 1990, devices are subject to use reporting and certain devices in particular are also subject to postmarketing surveillance and device tracking.

User reporting requires certain health care facilities to report incidents that suggest that a medical device has caused or contributed to the death of a patient, or serious injury to, or serious illness of a patient, as soon as possible but no later than 10 working days after they become aware of the incident.

Postmarket surveillance (PMS) is required for certain devices (e.g., implants) introduced in commerce after a certain date. It is discretionary for other devices, if necessary, to protect the public health. PMS is designed to be a system that allows for the identification of potential problems with a device within a reasonable period of time after its market introduction.

In device tracking, the law requires manufacturers to adopt a method of tracking for certain devices. Manufacturers are to supply to FDA within a certain period of time the identity of the patients and the locations of the devices in order to implement a recall from the patient or a patient notification program. Manufacturers are to have written standard operating procedures in place for their tracking system. Manufacturers are also expected to perform audits on a statistically significant sample of their data base to show that the patients who have the devices can be located.

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GLOSSARY

alternative technology
Can refer to either the use of another technology or the use of no technology at all.

***appropriate* adoption and use of technology**
Technology playing a positive role in mitigating healthcare costs while enhancing the delivery of effective, quality care.

clinical efficacy
What a technology can accomplish in expert hands when correctly applied to a particular type of patient; the technology demonstrating that it does what it purports to do.

clinical effectiveness
In reference to efficacy, refers to a technology's performance in more general routine applications; refers to the medical technology improving patients' clinical status (mortality, morbidity) and use of the particular technology demonstrating an advantage over alternative technologies.

clinical trials
Technologies that show promise in the laboratory are then tested in humans; such human testing is generally referred to as clinical trials.

cost benefit
The costs of using a particular medical technology to achieve improvement in patients' health outcome are compared to both the costs and the achieved improvement in patients' health outcome resulting from the use of alternative technologies. In cost-benefit analysis both costs and outcomes are expressed in the same units; these units are nearly always monetary.

cost effectiveness
The costs of using a particular medical technology to achieve improvement in patients' health outcome are compared to both the costs and the achieved improvement in patients' health outcome resulting from the use of alternative technologies. In cost-effectiveness analysis, costs are expressed in monetary terms and outcomes are expressed quantitatively.

device
Any physical item, excluding drugs, used in medical care.

diffusion
The movement of technology use from the research and development environment into general medical community application.

drug
A substance used as medicine in the treatment of illness or disease. Any chemical or biological substance that may be applied to, ingested by, or injected in order to prevent, treat, or diagnose disease or other medical conditions.

existing technology
Considered by providers to be a standard approach to a particular condition and diffused into general use.

GLOSSARY

Food and Drug Administration (FDA)
A regulatory agency for the development of regulations and product standards; development of methodologies and protocols for evaluation of product safety and efficacy; and approval of drugs, medical devices, and other products prior to marketing. Although the FDA reviews evidence accumulated in assessments directed by product sponsors, the agency does not conduct clinical trials of medical products. FDA assessment requirements address safety and efficacy but not cost, cost-effectiveness, or broader social issues. Sponsors must show their products are safe and efficacious as claimed in their labeling, but they are not required to show safety and efficacy relative to similar products.

healthcare industry
Medical device companies, pharmaceutical companies, biotechnology firms, hospitals, health professionals, health maintenance and insurance organizations, and others involved in the research, development, manufacturing, and distribution of healthcare-related services and products.

health outcome
Relates to mortality and morbidity factors as well as quality-of-life factors such as physical and psychosocial functional status, life satisfaction, and workforce participation.

investigational technology
Technology is in the clinical trial research stage to determine safety, clinical effectiveness, and improvement in patients' health outcome.

knowledge
The state or fact of knowing; comprehension acquired by experience or study.

net health outcome
A technology's beneficial effects on health outcome in comparison to its harmful effects on health outcome.

new technology
Past the stage of clinical trials but not yet in widespread use.

procedure (medical/surgical)
A practice of a health care provider that generally involves a combination, often quite complex, of special skills or abilities with drugs, devices, or both. In some cases, the drugs or devices involved are not predominant factors in a procedure. Instead, the technique of the provider performing the procedure is most important, such as in the performance of a surgical procedure facilitated by the use of scalpels, clamps, and drugs.

process
A system of operations used in producing something; a series of actions or functions that achieve an end or result.

professional judgment
Common sense. Professional judgment is particularly important when professional knowledge and hands-on-experience is available, and the scientific evidence is not.

GLOSSARY

provider
A professional or institution that delivers healthcare.

safety
A judgment of the acceptability or risk of using a technology in a specified situation.

technology
Medical technology includes drugs, devices, procedures, knowledge and/or processes applied to human health care.

technology assessment
Any process of examining and reporting properties of a medical technology used in health care, such as safety, clinical effectiveness, improvement in health outcome, cost effectiveness.

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TESTIMONY OF

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to the

103d Congress
United States House of Representatives

Committee on Small Business

Subcommittee on Regulation,
Business Opportunities, and Technology

October 21, 1993

Mr. Chairman and Subcommittee Members:

I am a full-time faculty member in the School of Medicine and the Wharton School, both at the University of Pennsylvania. In addition, I direct the University's Center for Health Policy, located at Penn's Leonard Davis Institute of Health Economics. I am a board-certified internist, but I spend the bulk of my time doing research and teaching in the areas of health policy, specifically health care technology assessment and physician behavior.

In the interest of full disclosure, I would like the Committee to know that my research has been supported by numerous pharmaceutical, biotechnology, and health care device manufacturers, as well as by private foundations and the federal government. In addition, I have acted as a paid consultant to all of the aforementioned entities. However, I am here today as a (hopefully) unbiased scholar, who spends a significant amount of time performing research related to the subject of today's hearing -- the adequacy of currently available information on the relative clinical performance and cost of medical technologies, and the potential of such information to reconcile the tension between health reform's twin goals of medical innovation and health care cost containment.

Another name for the subject of today's hearing is "the place of effectiveness research in health care reform." Effectiveness research is a field of investigation into the ways physicians actually practice, the ways patients actually behave and respond, and the ways to identify the true costs and benefits of medical interventions. New interventions that work well in theory or clinical trials do not always work as well in actual clinical practice because of poor patient compliance, high cost, untoward side-effects, or other reasons.

Currently available medical information does not focus on a sufficiently broad spectrum of outcomes, thus limiting the decision-making abilities of physicians, patients, and payers. The mandate of the Food and Drug Administration (FDA) has been to determine safety and efficacy, rather than cost-effectiveness and outcomes. This is necessary but not sufficient for making clinical and allocation decisions. Efficacy is defined as the ability of an intervention to do what it claims to do under ideal circumstances. As a result, significant time and money is being spent by drug and device manufactures to document efficacy. These studies are usually excellent, but they are done under very special circumstances (i.e., controlled clinical trials), in which patients are carefully selected, followed, and cajoled to use the new intervention in an ideal way. The research is highly protocol-driven; many tests and procedures are performed to make sure that the intervention is safe and doing what it is supposed to do. This limits the generalizability of these studies. Moreover, physicians are free to use drugs and devices in any way they choose after the regulatory approval process (there is no official approval process for medical procedures). This is necessary and desirable because patients don't present according to protocols. However, as a result, the true costs and benefits of new medical interventions as they are actually used in

actual clinical practice are not known for long periods of time, if they are ever known at all.

An effectiveness study, on the other hand, attempts to determine the actual cost and impact of a drug, device, or procedure in actual clinical practice. This is best done by collecting information from patients prospectively as they use the new intervention, without any external manipulations such as those included in protocol-driven clinical trials. Information can be sought from patients regarding, for example, their use of health care resources over time (to determine cost), the number of days of work lost with one intervention compared to another, quality of life differences between two interventions and, of course, the number of lives saved, life years saved, etc. These data can then be formulated into costs per effect or cost-effectiveness ratios in order to determine the best use of the health care dollar.

For example, consider medication for ulcers. Traditional medical research and development might investigate the theoretically important proxy of how much a new drug lowered the amount of stomach acid. In contrast, effectiveness-focussed research would evaluate actual events important to the patient, such as how well the new drug prevents clinically and economically apparent ulcers, rather than insignificant lesions that would not actually bother patients. Other outcomes of interest might be hospitalizations avoided, days of work loss avoided, impact on quality of life, and total costs over time.

It is difficult to recreate retrospectively, the true cost, value, and outcome of a medical intervention. Simulation or modelling techniques based on retrospective data have been used to approximate the true impact of medical interventions. These approaches are useful in making best guesses, and they are especially helpful when the net effect of an intervention is not expected for several decades, as in blood pressure or cholesterol control. However, these techniques are always open to question about the "best guess" assumptions that are a necessary component of this approach.

Although many observers are calling for wider use of effectiveness research, such as in the approval process for new technologies, the payment of physicians, formulary decisions, and determination of coverage policies, the effectiveness movement is in its early phases. Effectiveness research must be nurtured along with care, so that its implementation in the future can be valid, significant, and important, with the desired result -- an increase in health care value and what we can buy for our health care dollar.

Although outcomes research in the form of cost-effectiveness analysis has been mandated by regulation in certain other countries (e.g., Australia), it is the market place in the United States that is demanding better information on true outcomes. As we continue to move toward a more competitive health care environment, purchasers of

health care services are starting to demand information about the true total cost and the true outcomes of new interventions. In and of itself, I believe that this demand would eventually encourage most drug and device manufacturers to undertake good outcomes research. However, there is a problem with this approach. Manufacturers of drugs and devices currently are prohibited by the FDA from using most effectiveness information to market their products. They are restricted to marketing only on the basis of their approved FDA labelling, which often does not reflect how doctors practice. In addition, manufacturers currently are unclear about FDA constraints on the use of effectiveness materials. No one is certain about what is permitted and what is not. This is not an indictment of the FDA, because regulating outcomes information is not part of their mandate. However, this problem constrains the medical drug and device industry from responding to marketplace demands for more effectiveness information.

Incentives to facilitate outcomes studies by the drug and devices industry will help to encourage the quantity and quality of outcomes research that the marketplace needs and wants. However, the FDA or other regulatory agencies that grant such incentives must be clear about the ground rules. At a minimum, there should be regulatory relief so that drug and device manufacturers who produce high quality, valid, and reliable effectiveness information may use it in their marketing materials and in their negotiations with managed care, managed care formularies, hospitals, and other purchasers.

Effectiveness studies done after introduction of the drug or device into the medical marketplace are usually the most reliable, since they mirror actual, clinical practice. Therefore, it makes sense to provide extended exclusivity rights that would allow drug and device manufacturers to recoup some of the additional investment necessary to undertake post-approval outcomes studies. However, incentives should not be exclusive to those manufacturers who perform post-approval effectiveness work. Combining effectiveness research with preclinical studies also can be very fruitful, if done carefully and adjusted to account for the protocol-driven nature (by definition) of the studies. Companies should not be incentivized to postpone their effectiveness research only to the post-approval period. Therefore, regulatory relief and incentives to facilitate effectiveness studies must be comprehensive, covering both pre-approval and post-approval approaches. At a minimum, regulatory relief in the form of a consistent, simple policy toward the use of outcomes research in marketing would be extremely helpful in encouraging more outcomes research.

With respect to your specific proposal, it is essential that key terms be defined accurately. What is meant by "clinical studies" and "clinical superiority"? What is the threshold for a drug to be considered "significantly lower" in price? Since pre-marketing studies are constrained by protocol-driven trials, they do not necessarily deserve priority in terms of incentives, but should not be excluded from incentives either. Most importantly, any agency charged with awarding special incentives must be capable of evaluating effectiveness research, and clear about what the rules are. All effectiveness

analyses must be peer-reviewed prior to publication, just like in any true scientific endeavor.

In the short time that I had to prepare for this testimony, I could not reliably evaluate the total volume of currently available effectiveness studies, particularly cost-effectiveness studies. However, to the best of my knowledge, the majority of such studies currently are funded by the drug and device manufacturers themselves, compared to the government, the insurance industry, or academic centers (through voluntary efforts by their faculty).

The quality of comparative clinical outcomes studies, particularly cost-effectiveness studies, supplied by manufacturers of new drugs and devices historically has been mixed. Because manufacturers often are quite large companies with many subdivisions and frequent changes in personnel, it is not possible to point the finger at any one company, division, or person. Rather each study, undertaken by a specific division in a specific company headed by a specific person at a specific time should be judged by itself. In some cases, one company has sponsored extremely high-quality studies and extremely poor studies either simultaneously (from different divisions) or at different points in time. Researchers themselves also show some of these varied approaches to effectiveness research.

The problem is that, in contrast to FDA-regulated pre-marketing studies of safety and efficacy, outcomes research is unregulated, unstandardized, not necessarily peer-reviewed, and poorly understood, and pharmaceutical expertise and experience with this form of research is limited. Unfortunately, these of factors make it possible to produce "quick and dirty" studies without much chance of detection. On the other hand, many manufacturers have embraced effectiveness research with integrity and sound ethical behavior. Whereas the relevant studies of such an approach are generally valid, skepticism about manufacturer-sponsored effectiveness research, in general, places valid reports in jeopardy -- they are not viewed with the same credibility as traditional scientific research, simply because some companies and researchers (whether extramural or intramural) have taken advantage of the lack of oversight. Indeed, regardless of actual scientific validity of a study, the mere perception of potential bias has made end users of the research skeptical about the field as a whole.

I have attached a copy of my 1991 article in the New England Journal of Medicine to which you referred in your letter of invitation. The article describes in detail the challenges of industry-sponsored pharmacoeconomic research, an important component of effectiveness research. I believe that the problem of sponsor-imposed restraints on researchers involved in outcomes analyses has been more widely understood since the publication of my article, most of the issues raised currently remain unresolved.

Fortunately, 13 pharmaceutical and biotechnology firms are sponsoring a joint public-private-academic Task Force -- that I direct -- through "no strings attached grants" to the Leonard Davis Institute of Health Economics. This group is discussing and writing voluntary principles for the conduct and publication of effectiveness research related to pharmaceutical and biotechnology products. The Task Force is composed of individuals representing different stakeholder constituencies but, to facilitate the process and avoid bureaucratic delays, these individuals speak only for themselves. They are not formal representatives of any institution. Rather they are individuals with a great deal of knowledge about effectiveness research in the context of their workplace. The Task Force is comprised of "representatives" from government, trade organizations, academic medicine and medical ethics, private sector research, managed care, medical journals, and the pharmaceutical industry (three of the thirteen sponsor companies are represented at each of our meetings). We anticipate publication and dissemination of our results by next fall. While our efforts are focussed on pharmacoeconomics and cost-effectiveness research of new biotechnology products, the findings should be generalizable to industry-sponsored effectiveness research as a whole.

If incentives for company-generated comparative effectiveness trials are to be granted, the studies must be conducted according to the highest standards for scientific research. The Task Force has convened to begin to establish voluntary guidelines specific to effectiveness research. Effectiveness studies should follow these or equivalent guidelines and specifically state that they have done so. I believe that the marketplace can police itself, once such principles are established. If a company sponsors research and claims to have followed these principles, competitors will naturally attempt to validate these claims. A necessary regulatory requirement for this to work, however, is for full disclosure -- about whether or not the principles were followed and to mandate access to raw data when requested. Adherence to these suggestions will require disclosure of proprietary information by companies at certain times, further justifying the use of the type of incentives you are considering. Of course, the government may wish to charge one of its agencies to be vigilant for fraud and abuse in effectiveness research.

Payers in the new health care environment are going to have to learn to become more efficient, regardless of the form of health care reform that is adopted. Therefore, payers should not be expected to, nor be required to perform effectiveness studies, except as they meet their own proprietary needs in specific situations. Payers will not systematically evaluate new drugs and devices and it would be illogical to require them to do so, when one goal of health care reform is to create a more efficient health care marketplace with streamlined administration. To the extent that payers are involved in comparative effectiveness research, I am not aware of any specific systematic bias or inappropriate restrictions imposed on researchers. (However, I have not studied the situation carefully.) The rules and safeguards needed for participation of payers in these studies should be the same as those for manufacturers -- adherence to specific

principles for scientific integrity, including peer review of methodology, and full disclosure of methods and techniques. On the other hand, it is reasonable to call for dramatically increased federal research funding for effectiveness studies.

In summary, the clinical testing required by the FDA prior to approval for marketing produces high-quality scientific information about the safety and efficacy of new drugs and devices. Although these studies are useful for these purposes, they do not necessarily reflect how these drugs and devices perform in actual clinical practice, when they are subject to decision making by clinicians (who may prescribe for off label uses) and patients (who may decide when to take or if to take the drug or device as prescribed). Traditional studies do not address costs at all. It is precisely for this reason that effectiveness research is so important and why we must assure that its content is valid and reliable. High quality effectiveness information will facilitate the allocation of resources by payors, providers, and society. Creating an environment that nurtures this information is essential.

Thank you for your attention and consideration.

CONGRESS/63

SOUNDING BOARD

AVOIDING BIAS IN THE CONDUCT AND REPORTING OF COST-EFFECTIVENESS RESEARCH SPONSORED BY PHARMACEUTICAL COMPANIES

BECAUSE of the growing focus on containing health care costs, pharmaceutical companies are trying to demonstrate the cost effectiveness of their products relative to alternatives. In Europe and Australia, economic analyses are often required for government approval and pricing of new pharmaceuticals. In the United States, such analyses are increasingly being used for marketing and to obtain formulary approval. Because of the corporate need for timely results and confidentiality about a new drug in the period before marketing begins and because other financial support is limited, pharmaceutical companies themselves sponsor most academic research into the cost effectiveness of pharmaceuticals. The relationship is symbiotic. Academic researchers — especially young, unestablished investigators — are eager for new sources of funding.[1-3] At the same time, pharmaceutical marketing benefits from the imprimatur of research published by respected independent academic researchers.

We have performed 33 economic analyses for 15 pharmaceutical companies since 1978. Our experience indicates that the partnership between academia and industry in this research is often exemplary, generating important and valid new information. Sometimes, however, we have encountered difficulties that threatened to bias the conduct and results of an analysis. These problems represented potential conflicts of interest, because the sponsors of the studies benefit most from favorable results.

In this article we explore the conduct of industry-sponsored economic analysis. We offer examples of some specific biases that may occur because of the behavior of the investigator, the sponsoring company, or both. We explore whether there is a role for regulation by the Food and Drug Administration. Finally, we offer suggestions for structuring the relationship between industry and academia so that bias is minimized in economic analyses of pharmaceuticals.

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ETHICAL CONDUCT IN INDUSTRY-SPONSORED ECONOMIC ANALYSIS

The responsibilities of investigators in clinical research have been identified, evaluated, and debated in the literature.[4-8] Investigators' fundamental responsibilities are to conduct research and present results in an accurate and unbiased fashion.[4] Several sets of guidelines regarding fraud,[7-11] informed consent,[7-10] bias,[4,5,16] randomization procedures,[12,17] and other methodologic issues have been developed.[5] Ethical issues in industry-sponsored research include potential conflicts of interest between researchers and their funding sources,[4,18-27] the usefulness of industry-sponsored supplements to medical journals in which peer review is scant,[27] the responsibilities of academic centers in their partnerships with industry to develop proprietary patents and products,[4,28] and equity interests held by researchers in the companies sponsoring their research.[29] There has also been scrutiny of broader encounters between physicians and the pharmaceutical industry, including investigation of the content of continuing-education programs sponsored by pharmaceutical companies,[21,24] the use of company representatives as a primary source of information about new pharmaceutical agents,[30-33] and the ethics of promotional efforts by pharmaceutical companies, such as offering providers gifts, vacations, or free products.[22,34,35]

So far, however, the special case of industry-sponsored economic analysis of pharmaceuticals has escaped attention. Economic analysis is different from the clinical trials conducted at academic centers subject to FDA regulations. In contrast to clinical trials, economic studies generally use data and analytic methods of varying degrees of precision and power that are usually unstandardized, rather than standardized designs and analytic techniques used under the strict scrutiny of an external regulatory agency; involve subjective opinion and interpretation about what the results demonstrate, rather than limiting themselves to narrow conclusions about safety and efficacy; look at products selected by the pharmaceutical firms from among agents already (or nearly) in clinical use, rather than at all drugs for which FDA approval is sought; may make selective use of proprietary data gathered after marketing has begun, rather than disclosing all data by FDA requirement; and are funded and overseen most commonly by marketing departments, rather than medical or scientific divisions.

Pharmaceutical companies consider economic analyses to be marketing devices more than scientific or clinical research. This view raises problems related to differences in the missions of the sponsoring corporate departments and to the orientation and background of the people who oversee the research. Scientific personnel in pharmaceutical companies are accustomed to

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the ethics and issues of research methodology, whereas marketing personnel are concerned with the exigencies of the marketplace and the potential effect of economic findings on sales volume.

Economic analyses by academic investigators are funded by both grants to universities and contracts with them. Although some universities require that investigators follow strict rules to prevent conflicts of interest and protect academic freedom, such policies are neither universal nor uniform. Many economic analyses are performed without this oversight, by private research and consulting firms under a variety of contractual arrangements. Furthermore, economic analysis is a new, evolving, complex, and unstandardized field with which many editors, reviewers, policy makers, physicians, and universities are unfamiliar. Because economic analysis is poorly understood and unsupervised by an external agency, existing university policies to protect academic integrity are less able to detect and prevent bias in such studies than in other forms of research. Although the supervision of all types of clinical research may need strengthening, additional explicit guidelines are especially needed for economic analysis.

The Need for Guidelines

In economic analysis, the choice of which agents and interventions to compare, which data to include, which costs to measure, which perspective to adopt, which outcomes to assess, which assumptions to make, and how to present the results may produce important differences in a study's conclusions. For example, excluding subjects who do not respond, using charges rather than costs or payments, or not discounting outcomes can improve the calculated economic effect of an agent. When precise clinical data and information on price and use are unavailable, they must be estimated with statistical modeling techniques or expert opinion. Many of the assumptions made in economic analyses are not easily recognized by the readers of a study report.

In the absence of standardized methods, investigators may (consciously or subconsciously) design economic analyses to produce favorable findings, which may enhance future opportunities for corporate funding.[25,29] Investigators also prefer positive findings because they are easier to have published and command more attention than negative or marginal results among peers and the public.[13,16] Pharmaceutical companies, which generally prefer cooperative investigators to skeptical ones,[19] sometimes intimate (or suggest) the desirability of making the dollar impact of their product appear as favorable as possible. Inexperienced investigators with a limited perspective on research methods, ethics, and standards of practice and investigators who depend heavily on pharmaceutical funding may be most susceptible to these pressures.

Pharmaceutical companies' main interest in economic research is to promote sales. They therefore fund projects with a high likelihood of producing favorable results. Limited comparisons between products are sometimes authorized, but they exclude products that may compare favorably with the sponsor's own. Sometimes, only favorable clinical data are released to investigators. Pilot studies are commonly performed to assess the likelihood of favorable results before academic researchers are engaged to perform publishable independent studies. Some projects are funded in steps, so that losses can be cut if the initial results are not favorable.

Viewed as part of a company's marketing efforts, these represent good and well-accepted business practices. They systematically distort the balance of completed and published studies, however, since negative studies may be terminated before they are ready for publication. Indeed, published economic findings that are distinctly unfavorable to the sponsoring firm's product are rare, although companies are often disappointed when the answers are less favorable than anticipated. Some information about older, less cost effective pharmaceuticals is published because these are the agents with which companies generally want to compare their own products.

Many researchers, funding agencies, and journals prefer positive findings in any form of research.[13-16] Bias in economic analysis, however, leads to the systematic suppression of information about already available clinical agents with documented medical benefit but less favorable economic profiles. This bias is different from simply not undertaking the expense of a scientific investigation into a compound that is unlikely to have medical benefit in the first place. With economic analysis, any valid finding can potentially help decision makers determine the most appropriate use of an approved pharmaceutical (e.g., the subgroups of patients who should use the drug) or allocate resources more effectively.

Pharmaceutical companies, like other public or private organizations that contract for research, usually retain the right to review and comment on results and drafts of manuscripts before publication. Such reviews take various forms, with various degrees and styles of input. Input can often be helpful — for example, in facilitating the investigator's access to additional data, or in clarifying how a clinical trial was performed. In extreme cases, however, corporate personnel may seek to control the content and use of the final report, including the decision to publish. Investigators may be threatened with the withdrawal of current or future funding unless specific changes in methods, presentation, or results are made. Investigators may be without recourse if the company has stipulated that confidential data cannot be published when a contract has been terminated.

Bias may also result from an overemphasis on cost savings. A drug that increases costs may be more desirable than another treatment if the additional cost produces increased benefit and value. For marketing purposes, however, such a result is less compelling than results showing net cost savings. Investigators

frequently lose funding for potential projects when the prospects for cost savings (rather than mere cost effectiveness) are not promising.

Finally, pharmaceutical companies seek to sponsor economic analyses at a competitive price. The absence of regulatory oversight allows firms and investigators to compromise excessively in the inevitable trade-off between the cost and quality of a study. For example, the sample size needed to demonstrate an economic difference among pharmaceutical interventions is often larger than that needed to demonstrate clinical differences. Nonetheless, funding for economic analyses is often defined by the sample sizes involved in clinical projects designed to detect clinical differences.

In our experience, flagrant, intentional attempts by researchers or companies to manipulate results are rare, but other practices are not. For example, review of manuscripts before publication is usual, attempts to fund only positive studies are the rule, and incentives for investigators to make favorable assumptions are ever present.

Would Regulation Help?

Economic analyses are not currently required or reviewed by the FDA or any other regulatory body. Furthermore, although the few economic analyses sponsored by federal agencies (e.g., the Agency for Health Care Policy and Research, the Department of Veterans Affairs, and the National Institutes of Health) do include peer review of proposed methods before funding, projects sponsored by pharmaceutical companies are not subject to peer review until the material is submitted for publication. FDA oversight could help standardize the relationship between companies and investigators and reduce the potential for bias. Companies would be required to provide explicit funding from scientific departments for economic analysis, rather than including it in marketing budgets on a discretionary basis. The lack of a standardized approach to economic analysis would make additional FDA regulation cumbersome and controversial at this time, however, especially given the cost and delay it has introduced into the areas it already covers.

One type of bias is actually fostered by current FDA rules that restrict advertising to FDA-approved indications, which are based on the results of controlled clinical trials. Often, these trials do not reflect the ways doctors actually practice, because patient selection and monitoring in the trials are driven by protocols. When data (from studies undertaken after marketing has begun, for example) exist to indicate the effectiveness of a pharmaceutical in actual clinical experience, it may be desirable to assess the economic effect of the drug as it actually is used, not the effect of the FDA-approved uses alone. Some companies authorize economic components as part of clinical studies; in such cases, one arm assesses the behavior of patients and doctors outside protocol-driven constraints. Permitting the use of such results in marketing could help to ensure that economic analyses reflect both clinical realities and available clinical data.

Recommendations: A Protocol for Economic Analysis

Pressure toward bias is to be expected in a competitive marketplace. The selective production and presentation of results by one firm will provoke a competitive response from other firms. This impedes scientific progress by casting doubt on the objectivity and validity of results, whether favorable or unfavorable.[45] Identifying studies that have followed protocols designed to reduce bias would allow readers to recognize the likelihood of bias in studies not so designated. As a result, competitive pressures would be channeled toward less biased, more useful research. Adherence to these standards would generate a seal of approval that could in itself be valuable in selling pharmaceuticals in an increasingly skeptical and competitive marketplace. We offer the following eight recommendations.

First, written agreements between pharmaceutical companies and investigators should be in the form of research grants to universities, rather than contracts with individual investigators or universities. The agreements should stipulate that the researcher may publish findings regardless of their nature and retains sufficient access to proprietary data to allow publication even if funding is withdrawn. Such an arrangement will also ensure that questions raised by readers and other investigators can be addressed effectively. Private research and consulting firms should establish similar rules.

Second, economic analyses are by their nature comparative. The selection of alternatives to be compared should be based on their clinical relevance, not on the potential favorability of the results. At a minimum, comparisons required by the FDA for controlled clinical trials should be included. Research reports should be explicit about the comparisons chosen and those omitted. Data from all relevant studies, rather than a selected subset, should be made available to the investigator.

Third, investigators should be allowed to expand the company's study design to include additional types of costs, economic perspectives, and comparison drugs as data permit. If the funding group has placed constraints on an investigator, this information must be clearly disclosed to editors, reviewers, and readers.

Fourth, if projects are funded in a series of steps rather than by one large grant, results should not be provided to the sponsor until publication is guaranteed and funded. (Initial steps can include, for example, a review of the literature, general advice, and the planning of the economic model.)

Fifth, investigators should be vigilant to the temptation to produce favorable findings. The assumptions required in a study should be conservative (i.e., biased against the results sought by the funding company), clearly identified, and supported with formal sensitiv-

ity analyses. Editors should encourage the publication of these details despite current limits on the length of articles in many journals.

Sixth, investigators should publish valid results regardless of their promotional value to the sponsoring company, and journal editors should try to avoid a bias against publishing negative results.

Furthermore, researchers who receive a grant should not act as consultants on projects related to the study medication during the active period of the grant. Journals should require that all financial relations between authors and their sponsoring companies (as well as their direct competitors) be disclosed, including equity interests other than the ownership of shares in mutual funds.

Finally, researchers should take all reasonable steps to ensure that the level of funding permits methodologically sound, clinically relevant results with enough statistical power to detect important differences among the alternatives compared. Projects should avoid a "good enough for marketing" mentality.

All published studies should include a statement that their authors have adhered to this protocol. Universities and nonacademic researchers should develop and enforce standard agreements that meet these conflict-of-interest guidelines. Also, academic research societies, journal editors, pharmaceutical companies, and federal funding agencies should adopt these guidelines, perhaps after modification by a joint task force. Such actions will help ensure that this burgeoning new field of academic endeavor grows to fulfill its promise as a tool to help decision makers allocate resources effectively.

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Managing Care versus Managing Physicians--
The Critical Need for Better Information to Inform Practice Decisions

(All page references refer to the attached article)

Physicians at LDS Hospital in Salt Lake City, Utah, conducted a randomized clinical trial to compare a complicated, technology-intensive new treatment (Extra-Corporeal CO_2 Removal, or $ECCO_2R$) for Adult Respiratory Distress Syndrome (ARDS) to traditional ventilator support for the same condition. They demonstrated that ventilator management could achieve better patient outcomes at a lower cost, but only by restructuring the way in which they gave traditional ventilator support (pp. 13-18). Their experience illustrates several important principles about medical practice under health care reform proposals:

- Only 10—20 percent of common medical practices have a basis in scientific research. The remainder are based on tradition and anecdotal experience (pp. 20-21). That doesn't mean that 80—90 percent of medical practices are wrong—most of them probably do improve patients' health. But it does mean that practitioners can hold legitimate differences of opinion about which medical practices achieve the best results. Such differences of opinion extend into expert consensus panels and consensus guidelines (pp. 28-29).

- Difficulties in the dispersion of such scientific knowledge as does exist, complexity of medical systems, and documented human limitations to correctly synthesize complex information exacerbate the underlying lack of scientific knowledge (pp. 22-24). Eddy and Wennberg described the combined effects of these factors as "professional uncertainty."

- Professional uncertainty is the primary cause of observed wide variations in practice patterns. Such variation extends to both the decision to initiate treatment (Eddy's "practice policies") and the manner in which a treatment is carried out (Eddy's "performance policies"). For example, we studied six major conditions treated in hospitals (transurethral prostatectomy, cholecystectomy, total hip arthroplasty, coronary artery bypass grafts, cardiac pacemaker implantation, and community-acquired pneumonia). We found that physicians treating similar patients for the same condition varied from 60 to more the 450 percent regarding specific treatment decisions.

- Three potential benefits accrue from eliminating inappropriate practice variations: (1) Medical outcomes may improve; (2) costs may fall; and (3) stable practice patterns create an environment where it is possible to generate valid scientific knowledge for future practice improvements.

  [Note: Many experts question whether costs will truly fall as inappropriate variation disappears from clinical practice. We have done studies that show three causal mechanisms through which costs relate to quality.[1] The only issue is the extent of such quality/cost opportunities within American medicine and, hence, the scale of cost savings that may be possible through practice management. Estimates range as high as 40 percent of all health care costs.[2]]

- Stabilized care practices rest upon good clinical data (pg. 29). Physicians need valid information regarding appropriate processes of care and the outcomes they generate, for well-defined groups of similar patients in real practice settings, in order to eliminate inappropriate variation, improve outcomes, and reduce costs.

- Meaningful practice improvement requires a significant investment in both time and resources, but pay an even more significant return. Any successful program will require cooperation among medical technology suppliers and health care providers.

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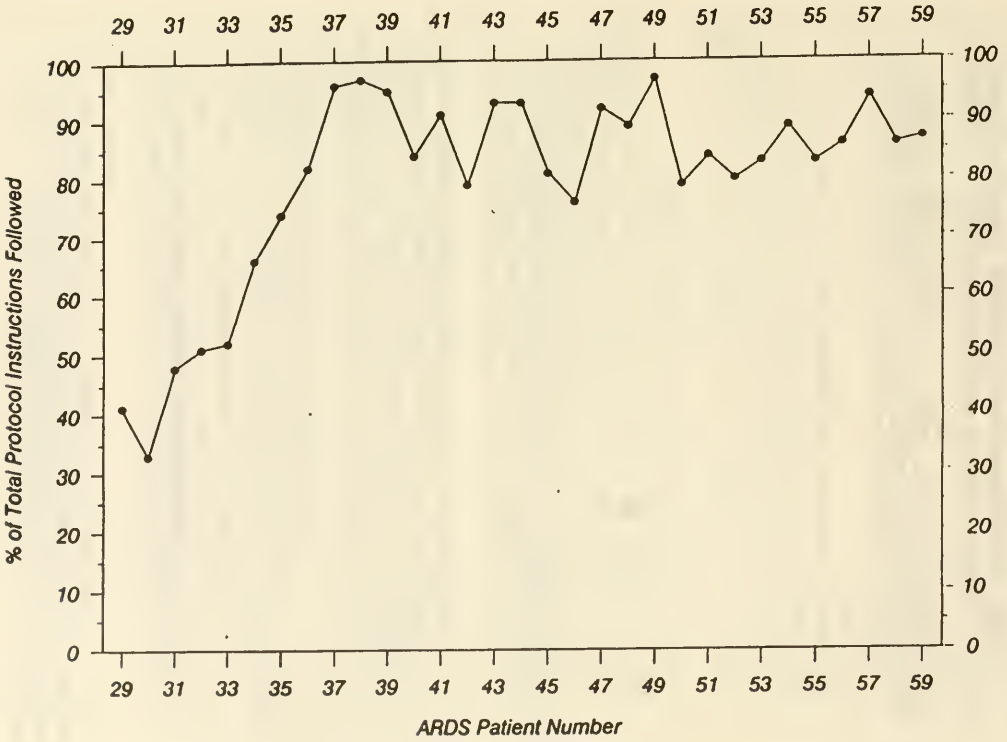
29 31 33 35 37 39 41 43 45 47 49 51 53 55 57 59
100 90 80 70 60 50 40 30 20 10 0
% of Total Protocol Instructions Followed
ARDS Patient Number

ARDS Protocol

- **Less physician time** (less "waffling")

- **Patients left the ICU faster**
  ("round-the-clock" management)

- **Much better survival:**

  - $ECCO_2R$: 38%
  - Stabilized ventilator management: 9.5 → 44%

- **Lower cost:**

  - $ECCO_2R$: about **$160,000** per case
  - Stabilized ventilator management: about **$120,000** per case

BRENT C. JAMES

Implementing Practice Guidelines through Clinical Quality Improvement

Summary

The American health care delivery environment is changing. As provider-at-risk payment strategies become increasingly dominant, they will force health care providers to replace old strategies that measured and managed revenues with new strategies that measure and manage costs. Quality improvement (QI) theory provides a set of tools to do exactly that—to understand, measure, and manage health care delivery processes and their associated costs. As a methodology for process management, QI theory merges case management, practice guidelines, and outcomes research into a single coordinated effort. It appropriately redirects management focus to care delivery processes, rather than to physicians. It also defines and illustrates a set of principles by which health care administrators can constructively team with physicians to find and document the best patient care outcomes at the lowest necessary cost, using QI-based practice guidelines as a decision support and measurement tool.

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American health care is changing. Ten years ago most American hospitals worked under a cost-plus system. Long-term financial survival required that a hospital's leaders manage *revenues*: They had to be certain that patients came to their facility to receive care (they tried to increase utilization) and they had to ensure that they added the right amount of financial margin to each service they provided. The natural unit of analysis in such an environment was a department. Many hospitals built sophisticated computer systems to track financial data at a departmental level, and used those systems as their primary source of management information and decisions. The medical staff bore responsibility for clinical quality, largely independent of administrators. Physicians also controlled the flow of patients into most hospitals. Therefore, hospital administrators often treated their medical staffs as their primary customers.

Then came 1983. That's the year the federal government first began to implement the Diagnosis-Related Group (DRG) Prospective Payment System (PPS). Suddenly, for about 30 percent of a typical hospital's case load, the size of the cost-plus margin no longer mattered. The government paid a flat rate per case regardless of the hospital's charges or costs. Hospitals initially shifted revenue shortfalls from government programs to other health care payer segments (a major factor in apparent hospital price inflation (Dranove, Shanley, and White 1991)). In response, many large private purchasers began to develop their own "provider-at-risk" strategies (i.e., managed care—per capita or per case payment) to limit health care expenses. Under those new structures, health care purchasers and third party payers began to supplant physicians' control of patient flow. Payers and patients became the hospitals' primary customers.

The medical staff bore responsibility for clinical quality, largely independent of administrators.

As the decade progressed hospitals saw larger and larger proportions of their patient volume shift to the provider-at-risk column. The phenomenon is most prominent on the west coast, where some community hospitals currently report that more than 90 percent of their inpatient volume comes through managed care contracts. It is gradually sweeping toward the east coast, engulfing localized pockets of heavy activity (such as the Minneapolis/St. Paul area) as it goes. And the trend is accelerating. For example, strategic planners at Intermountain Health Care (IHC—a 24 hospital system in Utah, Idaho, and Wyoming) initially estimated that provider-at-risk contracts would

increase from their current 60 percent penetration to about 85 percent of the system's total inpatient volume by the turn of the century. But vigorous political efforts to control health care costs, at both a national and local level, may reduce the time required to reach that level of managed care penetration to just three or four years.

As the provider-at-risk environment grows, hospitals are trying to use accounting adjustments to adapt their old revenue-based financial systems to the new reality. "Contractual allowance" or "deductions from revenue" measures what hospitals are *not* paid, relative to their charges. If managed care contracts account for most of a hospital's business, administrators can easily set their contractual allowance to any desired level by adjusting the hospital's charges, without affecting their net (real) revenues. In a provider-at-risk environment hospitals can no longer guarantee their long-term financial survival by managing revenues. Revenues are a fixed value, established through highly competitive, price-sensitive contract negotiations. Survival lies on the other side of the financial equation: Hospitals must begin to manage *costs*.

PROCESS MANAGEMENT

In a provider-at-risk, cost-based environment the natural unit of analysis and management is a *process*, not a department. A process is a series of linked steps, often (but not necessarily) sequential, designed to *cause* some set of outcomes to occur. The idea of a process not only aptly describes health care delivery but any repetitive human activity designed to add value, transform inputs into outputs, or cause some set of specified outcomes to occur. Processes usually span departments and facilities. Failures, which damage quality and increase costs, usually cluster around the interfaces, where one department or group hands off to another in the course of a single process.

Start with the idea of a process. Add to it fundamental knowledge of systems (processes interacting together), basic human psychology in a work setting, variation (statistics), and a theory for systematically acquiring and applying new knowledge (Deming 1990; Berwick 1993). Build a method to efficiently, effectively manage processes over time. The end result is the *methodology* (as opposed to the complementary philosophy) of quality improvement theory. In fact, implementing a total quality management strategy can be viewed as systematically redesigning a health system's infrastructure—its clinical data systems, financial data systems, human resources (policies and training), and culture—so that it is possible to manage and improve health care processes within a provider-at-risk environment.

Process management is also a common thread that brings together a number of current national health care initiatives: When focused on clinical processes of care, process management *is* case management. It blurs the line between operations and research, and provides a direct link between health care delivery systems and outcomes research (James, Horn, and Stephenson 1992). Finally, practice guidelines are explicit descriptions of preferred clinical processes. From that viewpoint practice guidelines are just a form of process management. Clinical quality improvement methods supply a set of tools to iteratively implement and modify such practice guidelines.

In 1989, the Congress of the United States formed the Agency for Health Care Policy and Research (AHCPR). Within its enabling legislation AHCPR has two specific missions: It must initiate studies to measure the outcomes of common health care interventions, and it must generate practice guidelines that codify research and consensus findings regarding best health care practices. These activities were mandated in the (untested) belief that they could eliminate inappropriate medical interventions and reduce health care costs (Institute of Medicine 1990). In addition to AHCPR, many professional groups, health care purchasers, and commercial enterprises are working to generate practice guidelines—often, though, with different objectives, different definitions, different levels of sophistication, and unequal quality in their final products.

Practice guidelines are explicit descriptions of preferred clinical processes.

It is hard to generate good guidelines. Special literature review methods, formal consensus techniques, sophisticated meta-analyses, and a very significant amount of effort are usually required. But many hospitals have the same hopes that prompted the U.S. Congress to launch AHCPR: They believe that, if they are to survive in the growing provider-at-risk environment, they must manage costs. They believe that practice guidelines may help them to document better patient care while controlling costs. Under many different names, hospitals therefore are trying to implement practice guidelines to manage health care delivery, whether they generate the guidelines themselves or obtain them from a third party.

The purpose of this article is to explore practical issues surrounding the physicians' role in the *implementation* of practice guidelines in American hospitals. It leaves the *generation* of practice guidelines to other sources (Institute of Medicine 1990; Eddy 1992). It also largely ignores the practical aspects of information systems and

organizational structures to handle the data associated with guideline implementation. With regard to physicians and guideline implementation, this article makes three key arguments to two crucial groups:

> **Physicians:** It is more important that you do it the same than that you do it "right."
>
> **Administrators:** It is more important how you implement than what you implement. The aim is to manage clinical processes, not to manage physicians.

To that end, this article first reviews several important quality improvement concepts central to any discussion that touches on cost, quality, and practice management. It then defines practice guidelines and introduces tools to document and manage them in a practical setting. It next presents a real-world case study in which a practice guideline was used to successfully manage a care process, simultaneously reducing costs and improving patient outcomes. Finally, it draws from the case study to discuss practical issues related to generating and implementing practice guidelines.

This article does not distinguish between *protocols* and *guidelines*—it uses the terms interchangeably. Many presently available guidelines (e.g., those published by AHCPR) lack sufficient detail to allow direct implementation. A potential user must first add a level of detail and definition that allows specific practice recommendations and measurement. With that level of detail a guideline becomes a protocol. But in terms of the physician relationships discussed here, the distinction is not critical.

Because of the physician focus of this article, all of the discussions and examples it uses center on clinical care delivery. But exactly the same techniques apply to nonclinical (administrative) support processes. Very often key clinical processes succeed or fail depending on the quality of the support processes upon which they rest. Further, it is not uncommon to find cost savings within administrative support processes that match or exceed those found in clinical processes. As a methodology, quality improvement and practice guidelines apply just as well to a hospital's administrators as to its clinicians.

IMPLEMENTING PRACTICE GUIDELINES: BACKGROUND PRINCIPLES

This article assumes that the reader is familiar with, and understands the implications of, several central principles of quality improvement theory. Those background principles are briefly outlined here, with

references that provide detailed discussions of their rationale and characteristics.

- *Quality controls costs.* Stated more accurately, quality and cost are two sides of the same coin. They are so tightly intertwined that it is impossible to act on one without acting upon the other (James 1989). Quality interacts with cost through three explicit mechanisms: Quality waste (costs fall as quality improves), productivity/efficiency (costs fall as quality holds stable), and cost-effectiveness (quality improves but at a higher cost). Quality also affects costs through secondary mechanisms such as the costs of attracting new customers, warranty (malpractice) costs, employee replacement costs, the costs of low employee morale, and long-term effects of low quality on an organization's standing within a community (the "ripple effect").

  Quality waste alone accounts for 25 to 40 percent of all hospital operating costs (Anderson and Daigh 1991). It is a particularly useful concept: As quality improves, it *causes* costs to fall—a very favorable combination for attracting new patients. The idea of quality waste also provides a means (by seeking waste and rework) to identify areas for improvement.
- People show a consistent, predictable response when confronted with data that purport to document substandard performance. Scherkenbach (1991) called that reaction *The Cycle of Fear* (James 1992). The first phase of the Cycle is *denial* ("kill the messenger" or shift the blame)—"my patients are sicker." During the second phase, those individuals being measured begin to *filter the data* ("game the system")—as they generate the data that others will later use to evaluate them, they change how they assess and record that information so as to cast themselves in a more favorable light. The final phase is *micromanagement*—they know that they are outliers, but have no idea how they came to such a position. They therefore try anything they can imagine that might improve their apparent performance. Even though the vast majority of such efforts are ineffectual, and though some may do active harm, at least they are showing a good effort.

  Many quality assurance programs bog down in the Cycle of Fear, devolving into meaningless measurement and reporting. In such situations the aim is to meet regulatory requirements—a subtly different goal than patient care improvement. Those being measured soon become cynical.

They lose all faith that the process can ever produce better patient care. More importantly, most of the energy expended on quality goes to arguments about methodology, rather than improvement.

- Traditional quality assurance uses thresholds (standards) to define acceptable and unacceptable performance. Providers who do not fall below the standard are judged "good enough"—their quality is acceptable. Most providers approach quality from that viewpoint, in order to pass regulatory review. But often it is possible to perform at levels far better than a standard that defines lowest acceptable performance. Every time a provider fails to be the best they can be, they harm their patients and they waste money (through quality's relationship to cost). Within health care *"good enough" is never good enough*—the only acceptable goal is to find, implement, and consistently perform the best possible care processes (James 1992).
- Finally, *"find and implement the best" is a more effective strategy than "find and eliminate the worst"* to improve patient outcomes and reduce costs (James 1992). It's not that traditional quality assurance doesn't work; it just doesn't work very well when compared to quality improvement. Two principles are involved in quality improvement: Process operators use measurement tools to (1) eliminate *inappropriate* variation (usually in care process steps) then (2) *document* continuous improvement (usually in outcomes). "Find and implement the best" redirects energy from finding fault (and the natural defensive response that it provokes) to finding solutions. It creates a much more positive atmosphere within which to measure, criticize, and improve health care processes.

IMPLEMENTING PRACTICE GUIDELINES: DEFINITIONS

In 1989, AHCPR commissioned the Institute of Medicine (IOM) to assess practice guideline development and evaluation. The IOM's 1990 report defined practice guidelines as "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances." The report catalogs many of the conflicting definitions of practice guidelines found in the medical literature and in practice, and attempts to distinguish among them. Eddy (1992) adds an important distinction to the IOM's

definition of practice guidelines. He defines *practice policies* as "preferred recommendations issued for the purpose of influencing decisions about health interventions." In contrast, *performance policies* (or clinical algorithms) "guide or review the performance of interventions, without concern for whether the intervention should have been performed in the first place." Practice policies describe "doing the right thing"—clinical indications that lead to a decision to apply a particular medical test or treatment. Performance policies define "doing it the right way." They describe the manner in which the test or treatment should be executed. Eddy further distinguishes three levels of practice policies, depending upon the degree of professional certainty about the outcomes of a particular practice and patients' preferences for the practice's predictable results: *Standards* describe practices with well-documented outcomes and virtual unanimity among patients about their desirability. A standard is a relatively strict rule that embodies a "best" clinical decision in essentially all circumstances. On that basis, deviations from standards should be rare. *Guidelines* apply to clinical interventions that have well-documented outcomes, but whose outcomes are not clearly desirable to all patients. They therefore should be followed in most cases, but must be modified for individual patients. Deviations from guidelines may be relatively common, as dictated by differences in individual patient circumstances. *Options* describe medical interventions for which outcomes are not known, patient preferences are not known, or about which patients are indifferent. Options are neutral with respect to recommending a particular medical intervention—they simply provide a list of credible choices.

Guidelines apply to clinical interventions that have well-documented outcomes, but whose outcomes are not clearly desirable to all patients.

Practice policies and performance policies are obviously tightly interlinked. Eddy (1992) notes that correct performance of an intervention is immaterial if that intervention is not appropriate. But patients and clinicians choose a particular practice based on its documented outcomes. Those outcomes cannot be accurately established if the practice is not performed correctly. Seen another way, the "decision to intervene" and the "performance of the intervention" are sequential steps within a single process, with patient outcomes completing a feedback loop to inform the initial decision. Guideline implementation centers on performance policies, but draws from practice policies for source material.

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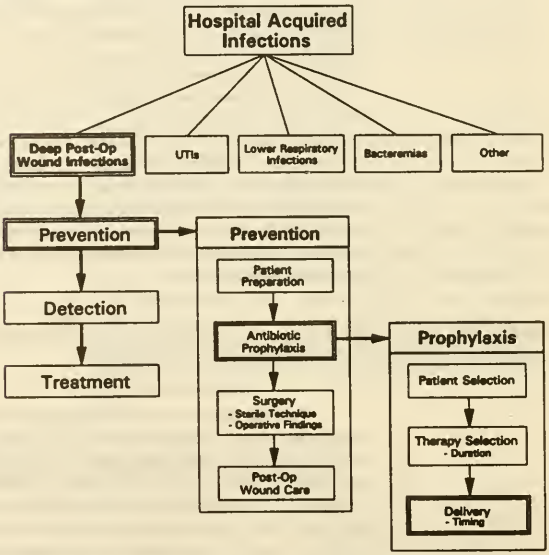
Flow charts are a generic tool to document processes (several medical publications have recommended flow charts as a professional standard for recording, comparing, discussing and systematically improving practice guidelines](Society for Medical Decision Making Committee on Standardization of Clinical Algorithms 1992; Pearson et al. 1992; Hadorn, McCormick, and Diokno 1992). When a guideline is laid out as a flow chart, an important feature found in all processes becomes evident: Processes are inherently hierarchical. In other words, every box in a flow chart hides another, more detailed, sub-flow chart.

To illustrate, Figure 1 shows the process used at IHC's LDS Hospital (in Salt Lake City, Utah) to manage deep post-operative

Figure 1. Hierarchical Process of Care



A flow chart describing a hierarchical process of care used to manage deep post-operative wound infections. Such flow charts can be used both to control complexity when describing a clinical process, and to identify appropriate measurement points to monitor critical care processes. In some instances the simple act of documenting a process flow will improve coordination and reduce variation among care providers.

wound infections. Each step in the highest level process (Prevention → Detection → Treatment) is the outcome of a subprocess, with its own series of steps. Similarly, each step in every subprocess is the outcome of an even more detailed sub-subprocess, and so on down to an arbitrary level of detail. That means that every box in a flow chart is both a process step (of its superior process) and an outcome (of its subprocess). The terms "outcome" and "process step" are interchangeable, depending on the level of abstraction employed to manage a particular subprocess at a particular point in time. Hierarchical flow charts are useful tools to focus attention and manage complexity. Starting with a high-level flow chart, detail is added within a focused area by expanding appropriate subprocess flow charts. When detail is no longer needed, the subprocess flow charts are collapsed back into their superior process steps. Flow charts play another essential role: They are the foundation for effective communications and systematic improvement within a clinical team. Without a written paradigm, differences in mental models, perceptions, and terminology make it extremely difficult to even discuss a complicated care process. With a written model guideline team members can identify differences in practice style, criticize specific steps in the model, and recommend improvements. Finally, when monitoring a clinical process, a flow chart identifies measurement points. It shows the data that are needed to track both performance and outcomes within a particular process.

Without a written paradigm, differences in mental models, perceptions, and terminology make it extremely difficult to even discuss a complicated care process.

Decisions (practice policies) and execution (performance policies) are embedded throughout a clinical flow chart. For example, the use of Antibiotic Prophylaxis is the second performance step in the Prevention subprocess for deep post-operative wound infections. But the first step in the Prophylaxis subprocess is Patient Selection. That step requires a decision. Clinical indications (a practice policy) identifies patients who should receive prophylaxis. Collecting and evaluating the information necessary to decide whether to use prophylaxis for a particular patient is a process in itself, with its own decision and performance steps. Nearly every performance step depends on underlying decisions, while nearly every decision step depends on underlying performance.

Eddy (1992; 1990–1992 (series)) has championed the use of meta-analytic methods to extract and synthesize important scientific information to guide clinical decisions. His work provides a critical

service in those instances when scientific data are available. Leape, Kosecoff, Chassin, Brook and other researchers at RAND have developed formal consensus techniques for use when scientific data are not available (Park et al. 1986). But given a practice guideline that describes a performance policy, based on appropriate practice policies, how can a hospital work with a clinical team to manage the process and document (for patients, purchasers, and regulators) that effective, efficient care results?

IMPLEMENTING PRACTICE GUIDELINES: A CASE STUDY

Adult Respiratory Distress Syndrome (ARDS) is a disease of the lungs. It often appears as a complication of an underlying pneumonia or shock and multi-organ failure. For example, one common precipitating cause is a simple viral pneumonia—a chest cold, of the sort that many individuals experience during the winter. For reasons that are not clearly understood, some patients' lungs react to the pneumonia by secreting fluid into their air spaces. As the lung's air spaces fill with fluid the lungs are not able to move oxygen into the blood (hypoxemia). The fluid also makes the lungs stiff (noncompliant), difficult to inflate and deflate as the patient breathes. Traditional treatment depends on mechanical respiration (ventilator support), with high oxygen concentrations and constant high air pressure to force oxygen into the blood despite the fluid. If the patient remains alive until the underlying pneumonia or shock resolves then their ARDS will often clear. Those who live usually achieve a complete recovery and regain normal health.

While ARDS affects both genders and all ages, it concentrates mainly within young men, in their twenties and thirties. Each year it accounts for about 15,000 cases in the United States. Historically, among all patients who developed ARDS only about one third survived.

During the mid-1970s pulmonary researchers developed an alternative therapy to use in place of stand-alone ventilator support. Called extra-corporeal membrane oxygenation (ECMO), it used a heart-lung machine, connected through the patient's femoral artery and vein, to oxygenate the patient's blood outside their body. In theory, that would keep the patient alive until their underlying pneumonia or shock resolved and their ARDS cleared. The researchers also established metrics (the ECMO criteria) that identified a subgroup of ARDS patients who were at a particularly high risk for death. Historically, about ten percent of patients who met the ECMO criteria survived. Clinical trials conducted on patients who met the ECMO criteria eventually demonstrated that ECMO was no better in

preventing ARDS deaths than standard ventilator therapy. The ECMO therapy was therefore abandoned. But pulmonary researchers have continued to identify and track ARDS patients who meet ECMO criteria. Recent estimates of survival among ARDS patients who meet ECMO criteria reach as high as 15 percent.

In the 1980s an Italian pulmonary research group reported a variant of ECMO that they claimed significantly improved survival in ARDS patients. In addition to oxygenating a patient's blood outside the body, they added equipment to simultaneously remove CO_2 and other waste products (extra-corporeal CO_2 removal, or $ECCO_2R$). A pulmonary research team at LDS Hospital received a grant from the National Heart, Lung, and Blood Institute to test the new therapy in the United States. They planned a randomized clinical trial to compare $ECCO_2R$ (the treatment arm of the trial) to standard mechanical ventilation (the control arm) for ARDS patients who met ECMO criteria.

A key factor in clinical trial design centers around the idea of consistency. If a clinical trial is to accurately compare two competing treatments, then each of the treatments must be applied in a consistent fashion. Otherwise it is impossible to judge whether differences in patient outcomes are due to the treatments or to variations in their application. Trials therefore usually use protocols to describe, in detail, the manner in which each treatment will be delivered. As the LDS Hospital research team began to construct the $ECCO_2R$ clinical trial they had an important insight: They recognized that, despite the fact that they had practiced together for many years, cross-covering each other on the same patients, they didn't manage ventilators in a consistent fashion. Those differences went beyond variation among the physicians, nurses, and therapists in the group. Individual clinicians showed differences in practice patterns from patient to patient. In fact, it appeared that a single clinician sometimes was inconsistent when treating the same patient from day to day, or even from morning to evening rounds.

If a clinical trial is to accurately compare two competing treatments, then each of the treatments must be applied in a consistent fashion.

The team therefore decided to generate a detailed protocol—a practice guideline—to oversee ventilator management on the control arm of their clinical trial. They first performed a careful literature review to identify important research findings that should guide their decisions and care practices. They then used formal consensus

techniques to fill in those parts of the guideline not covered by the scientific literature, and represented their new guideline as a flow chart. It described ventilator management for ARDS in detail, being more than 35 pages long with an average of more than twenty major decision nodes per page.

But when they had completed the guideline they had a second important insight: Much of their new ventilator management guideline was based upon consensus—"expert" opinion, generated as a theoretical exercise far from the treatment of real patients. They had no *data* to demonstrate that the consensus portions of their guideline were correct. Because of the consensus process, they had no scientific basis to argue that the guideline represented best care for real patients.

The ECCO$_2$R team therefore chose to use their new ventilator guideline in a very innovative way. They reviewed the guideline with all involved clinicians (nurses, physicians, and other allied health professionals) so that everyone understood its content. They built a measurement system to track whether the clinicians followed the guideline's recommendations, at the level of each detailed decision covered in the document. Finally, they placed a copy of the guideline at the bedside of every ARDS patient being treated with a mechanical ventilator, and asked that the clinicians follow it. But if a clinician disagreed with a guideline recommendation, the team instructed the clinicians to follow their own judgement, not the guideline. In such circumstances they assumed that the guideline was probably wrong, not the clinician. After all, they knew and trusted the clinicians on the team. It was the guideline that had yet to prove itself with demonstrated results.

The research team then carried their reasoning to the next logical step: If a clinician failed to follow the guideline, leading to the assumption that the guideline was probably wrong for that particular decision, then they had an opportunity to correct the guideline. They therefore automatically added that clinical case and the associated guideline-based decision to the agenda for their next weekly staff meeting. That meant that they were able to discuss each questionable guideline recommendation as a group, in the context of a real case. In those meetings they stripped identifying information from the cases in order to avoid the Cycle of Fear. Their aim was to fix the system, not fix blame. They wanted to agree upon a "best" treatment processes as a group, not single individual team members out for criticism.

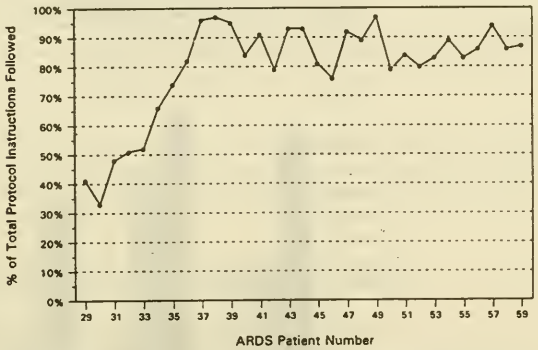
Three possible courses of action are possible in such a setting:

1. As the team examined a guideline recommendation, they could conclude that the guideline was wrong and change it.

2. The team could agree that the guideline was right. That sends a message not only to the clinician who had made the original decision, but to all members of the team, concerning their group consensus about best patient care, as codified in the guideline.
3. They could decide that the case was an outlier for that particular decision. No guideline can reasonably cover all patient variants.

Figure 2 shows guideline compliance rates as the team used their iterative review process (Henderson et al. 1990). Over a period of about four months, guideline compliance increased from under 40 percent to more than 90 percent (Henderson et al. 1992; Henderson et al. 1990; East et al. 1992a). In the early stages changes to the guideline were common. Note that the team never achieved perfect

Figure 2. Ventilator Protocol Compliance (9/14/88–1/20/90)

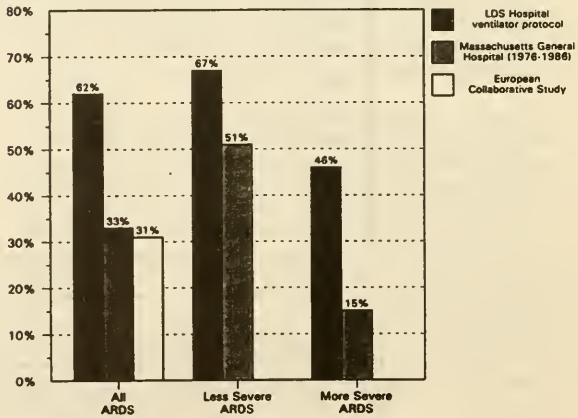


Percentage of protocol-based recommendations followed for Adult Respiratory Distress Syndrome (ARDS) patients, starting with the first patient (Patient Number 29, admitted to LDS Hospital's Pulmonary ICU on August 14, 1988) for whom the protocol was used through 30 consecutive patients (Patient Number 59, admitted on January 1, 1990). A typical treatment episode involved more than 200 protocol-based treatment recommendations. Roughly four months elapsed between Patient Number 29 and Patient Number 37. From Patient Number 37 on, most protocol noncompliances occurred either (1) when a patient was removed from the ICU (usually for either surgery or imaging), (2) as further improvements to the protocol were tested, or (3) as a consequence of the fact that few protocols are perfect (nearly all guidelines show some level of random noncompliance as clinicians address patient factors not anticipated by the protocol or factors that are so rare as to not justify inclusion in the protocol).

guideline compliance. No guideline will ever perfectly match every patient, or supplant clinical judgement (East 1992b). Statistical process control (SPC) provides an ideal tool to track noncompliances in a process, separating treatment deviations arising from differences in patient presentation (appropriate, common, or random variation) from those arising from external practice patterns that intrude into the treatment process (inappropriate, special, or assignable variation) (Ryan 1989).

Upon completion of the randomized clinical trial, $ECCO_2R$ achieved 38 percent survival for patients who met ECMO criteria. Stabilized ventilator management (as produced by the ventilator protocol) achieved 44 percent survival for the same patient group, better than the $ECCO_2R$ treatment arm and much better than the 9 to 15 percent survival expected for ventilator management from historical experience (Morris et al. 1992; Morris 1992). Figure 3 compares ARDS survival experience from several pulmonary research groups, covering cases beyond the LDS Hospital $ECCO_2R$ clinical trial (Zapol et al. 1991; Artigas et al. 1991).

Figure 3. Percent Survival for ARDS Patients



Survival among Adult Respiratory Distress Syndrome patients by risk class, comparing LDS Hospital's experience with stabilized ventilator management (a detailed practice protocol) with that of other major pulmonary research groups who did not use the ventilator protocol.

The team's experience with a practice guideline produced other interesting results:

- Physician time to manage these complex cases fell. That was because common, day-to-day decisions were pushed down into the system, where physicians did not have to consider them one case at a time. It wasn't that the physicians didn't think about the patient care issues involved, but that they addressed them for groups of patients, instead of case by case. That freed physicians to deal with the patients' interesting problems, that required a physician's oversight, or allowed the physician to see other patients. It also made the members of the team (physicians, nurses, and technicians) more predictable to one another, which may reduce friction and improve efficiency.
- If a patient lived, they may have left the intensive care unit (ICU) faster than similar patients had before the introduction of the ventilator protocol. That is probably because the patients could advance on the protocol 24 hours per day, rather than waiting for a physician to come on rounds and change orders.
- Stabilized ventilator management cost about $120,000 per patient who lived. $ECCO_2R$ (the next best therapy) cost more than $160,000 per patient who lived, not counting physician fees.

The LDS Hospital pulmonary research team is now supervising a follow-up randomized clinical trial that compares traditional ventilator management for ARDS patients to stabilized ventilator management as produced by their ventilator protocol.

IMPLEMENTING PRACTICE GUIDELINES: LESSONS LEARNED

Lesson 1: The core problem is variation in clinical practice.

When members of the LDS Hospital ARDS research team recognized the variability of their own ventilator management practices, they built upon a long line of studies that demonstrate variation in medical practices. Glover first measured differences in the rates of tonsillectomy among various regions of England, beyond what could be explained by population differences, in 1938. Lewis provided additional evidence of the phenomenon in the United States in the late 1960s.

During the 1970s and 1980s, Wennberg formalized and extended analytic techniques for examining differences in surgical procedure use rates or hospitalization rates among communities. He called those methods small area variation analysis (SAVA). His studies again demonstrated that hospital admissions for some surgical procedures and medical diagnoses occurred at a much higher rate in some communities than other, similar communities, even after controlling for underlying population factors (Wennberg and Gittelsohn 1973; Wennberg 1985; Wennberg, Barnes, and Zubkoff 1982). Wennberg also showed that the range of inter-community variation was related to specific surgical procedures and medical diagnoses. When examining the rates of use for the same procedures and diagnoses in other countries, he found that some showed consistently low ranges of variation within all countries examined, while others showed consistently high ranges of variation within all countries examined. This was true even though the average use rates for each procedure or diagnosis varied significantly between the countries included in the study (McPherson et al. 1982).

The RAND team developed formal methods to generate measurable indications for several surgical procedures and medical hospitalizations.

The RAND team (Park et al. 1986) hypothesized that SAVA differences among communities could be explained by higher rates of inappropriate treatment in communities with high use rates. The RAND team developed formal methods to generate measurable indications for several surgical procedures and medical hospitalizations. For each condition they examined, they first performed a structured review of the medical literature. They then presented the resulting scientific information to a panel of expert physicians, drawn from the appropriate specialty area. Within each expert panel they used formal consensus techniques to derive extensive lists of appropriate, equivocal, or inappropriate indications for the treatment under study. Finally, they used their indications to measure the rates of appropriate versus inappropriate use of the targeted conditions in communities that showed high rates of utilization and communities that showed low rates of utilization for the procedure or hospitalization in question. They discovered that high use rates were not consistently associated with high rates of inappropriate indications (Leape et al. 1990). That is, geographic areas that showed low utilization rates for a particular surgical procedure or medical hospitalization often had as high a rate of inappropriate indications as other geographic areas that showed high

utilization rates for the same medical decision. They also demonstrated that inappropriate surgical procedure use and inappropriate hospitalization for medical conditions are surprisingly common, and that some procedures or hospitalizations show consistently high rates of inappropriate application, while other show consistently lower rates of inappropriate use (Brook et al. 1990; Winslow et al. 1988).

Wennberg's small area variation analysis and the RAND team's measures of appropriateness addressed a single class of issues: Both examined the decision to treat a patient, at the level of Eddy's practice policies (indications for treatment). A further set of studies (James et al. 1987, 1988) investigated variations in what happens to patients after they enter a hospital (at the level of Eddy's performance policies). Their Quality, Utilization, and Efficiency (QUE) studies tracked patients with comparable presenting disease, comorbidities, and outcomes hospitalized for transurethral prostatectomy (TURP), cholecystectomy, total hip arthroplasty, and permanent pacemaker implantation (Baird et al. 1988, 1989). Those studies showed that physicians used widely different amounts of specific care factors to treat similar patients, with differences among physicians ranging from 60 to 460 percent. Figure 4 illustrates two important process of care factors for TURP—true surgical procedure time and grams of prostatic tissue removed—among 16 urologic surgeons, across a group of comparable patients at four hospitals. Each factor varies by more than 200 percent across the physician group.

While well-designed studies document wide variations among physicians with regard to their decisions to apply treatment to patients and the manner in which those treatments are applied, anecdotal information suggests that practice variation may extend even further. Individual physicians appear to vary in how they diagnose and treat similar, sequential patients, beyond what would be expected from patient factors. Observation of very complicated patients (for example, ARDS patients on ventilators as described in the case study) suggests that physicians may vary from contact to contact, morning to night, in how they treat individual patients.

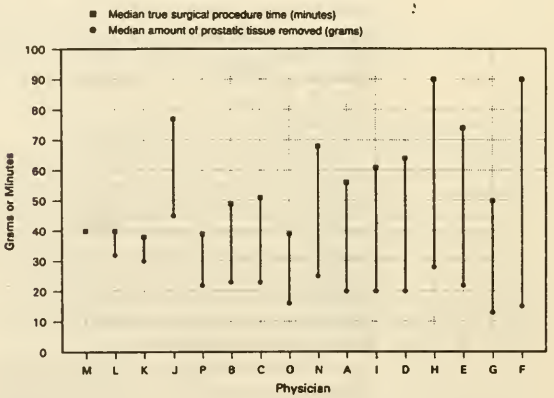
Eddy, Wennberg, and others have summarized possible causes of practice variation (Eddy 1984; Eddy and Billings 1988; Wennberg, Barnes, and Zubkoff 1982; James, Horn, and Stephenson 1992). The combined list is extensive, running to more than 60 different items. Interestingly, many of the most prominent causes are not under physicians' control. They arise from professional uncertainty:

- *80 to 90 percent of common medical practices have no basis in published scientific research.* In 1979, Williamson tracked

common medical practices for three subspecialties of internal medicine back to the medical literature. He estimated that fewer than 10 percent of the medical practices examined had any foundation in published research (Williamson, Alexander, and Miller 1968; Williamson, Goldschmidt, and Jillson 1979). Follow-up studies by the federal Office of Technology Assessment in 1985 (Bunker 1988; Institute of Medicine 1985), and the Office of Medical Applications of Research in 1990 (Ferguson 1991; Dubinsky and Ferguson 1990), generated estimates of 10 to 20 percent and less than 20 percent, respectively.

That does not mean that 80 to 90 percent of medical practices are wrong. They are based on a long history of medical tradition and experience, and probably help most

Figure 4. Variation in Transurethral Resection of the Prostate (TURP) Practice Patterns among 16 Urologists



Variation among urologic surgeons for two important process of care factors when performing a transurethral prostatectomy (TURP): true surgical procedure time and grams of prostatic tissue excised. The cases in the study were similar in terms of the presence and severity of comorbidities on admission to the hospital and in terms of medical outcomes (complications and therapeutic goals). The surgeons are shown in order of grams removed per minute of surgery. Both factors (surgery time and grams of tissue) showed more than two-fold variation across the physician group. The length of surgery had a strong statistical association with grams of tissue removed: The longer a surgeon's procedure time, the smaller amount of tissue removed.

patients. But it does mean that for most medical practice we do not know what is best. Practitioners can hold legitimate differences of opinion about best practices.

- *Much of the scientific research that does exist is not available to medical practitioners.* Williamson et al. also documented that even when scientific research regarding best medical practices does exist, its diffusion into actual medical practice is slow and uneven (Williamson, Alexander, and Miller 1968; Williamson, Goldschmidt, and Jillson 1979). Given the size, complexity, and lack of methodologic consistency of the medical literature, that finding is not unexpected. An effort to find, evaluate, and synthesize appropriate scientific articles for a particular medical topic requires special expertise. Most practitioners lack the tools, resources, and time for such an undertaking. Williamson, Lincoln, and Turner (1991) recommended a set of formal methods (called information synthesis) for that purpose (Goldschmidt 1986). Eddy has published meta-analytic techniques, and produced and distributed computer software, to address the same issue (Eddy 1992; Eddy, Hasselblad, and Shacter 1992).
- *Even such limited scientific information as is available may overwhelm the capacity of the unaided human mind.* The human mind is limited in its capacity to synthesize complex information to optimize outcomes. When working with the ventilator guideline presented in the case study, Morris (1992) found that experienced physicians were not able to manage more than four concurrent variables to maximize patient outcomes. Unfortunately, a typical ARDS case presented more than 200 active variables. A physician's patient care decisions depended on which small subset of variables the physician chose to analyze. As different variables thrust themselves into the physician's attention at different points in time, the physician's practices changed. Thus, a physician could vary from morning to evening in managing the same patient. While ventilator management for ARDS patients in an ICU is admittedly complex, most patient care decisions involve far more than four variables.

American medical practice is based on the notion of a physician-patient relationship. That ideal asserts that best patient care occurs when an individual physician advises a patient on factors affecting their physical and mental well-being, available health care responses, and likely outcomes, so that the patient can make informed decisions about their own health. A major corollary is the assumption that an

individual physician can *subjectively* integrate hundreds of disparate factors to accurately advise patient decisions. At a minimum, a physician must correctly synthesize the patient's underlying disease processes, their individual physiologic response to each of those diseases, various treatment options, likely outcomes for each possible treatment, and the patient's personal values and preferences, in order to provide an accurate list of options from which the patient can chose. But that model is incompatible with knowledge of the limited capabilities of the unaided human mind.

Perhaps Eddy (1990, no. 4) said it best: "It is simply unrealistic to think that individuals can synthesize in their head scores of pieces of evidence, accurately estimate the outcomes of different options, and accurately judge the desirability of those outcomes for patients. . . . All confirm what would be expected from common sense: The complexity of modern medicine exceeds the inherent limitations of the unaided human mind."

- *Humans are inherently fallible information processors.* McDonald (1976) demonstrated that, regardless of training or intent, humans make errors when handling data. Some types of errors, such as digit transpositions when writing numbers or misplacement of decimal points, occur more frequently. An individual's error rate is affected by stress levels (e.g., lack of sleep), complexity, and whether that individual is operating within their domain of specific knowledge. Simple errors can introduce variation into patient care. Carefully designed, robust processes can catch and correct or reduce the effect of human errors when they do occur.
- *Differences in observation—measurement error—can lead to differences in assessment and differences in treatment among physicians.* Koran documented frequent differences among physicians in physical examination findings, interpretation of diagnostic procedures, diagnosis, recommended treatments, and evaluations of the quality of care (Koran 1975). He notes, "The physicians studied almost always disagreed at least once in 10 cases, and often disagreed more than once in five cases, whether they were eliciting physical signs, interpreting roentgenograms, electrocardiograms or electroencephalograms, making a diagnosis (from incomplete information), recommending a treatment or evaluating the quality of care. Disagreements of this magnitude, if characteristic of clinical practice in general, cannot safely be regarded as inconsequential."

Beyond differences in patient care that arise from professional uncertainty, human limitations, unequal allocation of health care resources, and variation in measurement, patients differ from one another and individually differ over time. Among other inconsistencies, they have different values, different preferences, different symptoms, different physiologic response to disease, and different ways of interacting with health care providers. All of these factors cause appropriate differences in practice patterns. Any clinical process management system must group patients together in a way that takes those differences into account.

Lesson 2: Real benefits accrue to patients, payers, and providers when *inappropriate* practice variations decline.

Quality improvement uses statistical process control to separate *assignable* from *random* variation. Random variation arises from differences in a process's inputs (i.e., differences in patient presentation) or the sum of many small variations in process steps that cannot be tracked to specific, preventable causes. It is a physical, measurable attribute, representing the random noise in any real process. Assignable variation arises from identifiable causes that can be tracked and eliminated. Statistical process control graphs the probability that variation in a specific process measurement arises from assignable, rather than random, causes. In quality improvement jargon, assignable variation represents *inappropriate* variation. Random variation is not only appropriate, but expected. When it does not appear something is probably wrong.

It is important to distinguish between the two types of variation because each requires a different management approach. With assignable variation, the aim is to track the outlier points to their root causes then eliminate them, so they never intrude in the process again. On the other hand, random variation is a physical attribute of the process and its inputs. To reduce random variation, a provider must design a new process (usually a variant of the old process, generated by changing specific process steps), then scientifically compare its performance against the old approach. Quality improvement theory calls such a test the Shewhart Cycle, and summarizes its steps as "PDCA": Plan a change, Do it in a small subgroup, Check its performance against prior outputs, then Act (discard the change or fully implement it). Traditional medicine calls the same approach a clinical trial.

Quality improvement theory defines a *stable process* as a process that shows only random variation over time, with no assignable variation. *Process capability* is the ability of a process to achieve

its stated goals. For example, a process designed to prevent infections has an absolute goal of no infections. If only two percent of cases develop infections, then the process is 98 percent capable—it achieves its goal 98 percent of the time.

Quality improvement theory notes that it is impossible to measure a process's true capability unless that process is stable. Otherwise, variation in performance can alter (for the worse) the apparent efficacy of the process (the actual outcomes of an uncontrolled process in a community setting is called effectiveness). That is exactly the same idea embodied in the treatment protocols that define each arm in a controlled clinical trial. Such protocols guarantee that the trial's treatments are consistent from case to case. Otherwise, it is impossible to tell whether differences in patient outcomes arise from true differences in the capabilities of the treatments, or just variation in how they were applied.

In other words, if a clinical process shows inappropriate variation, it is impossible to even measure its true outcomes, let alone apply the scientific method (clinical trials) to systematically improve. But American medicine is rife with assignable variation. Much of it arises from practice differences among physicians. But for 80 to 90 percent of common medical practices, physicians' assertions of what is "right" for their patients is just a matter of opinion.

Quality improvement theory notes that it is impossible to measure a process's true capacity unless that process is stable.

Hence the statement to physicians regarding their patient treatment practices: It is more important that you do it the same than that you do it "right." For when, as a group, physicians develop consistent practices based on the best scientific information and peer consensus, they can accurately measure patient outcomes and apply the scientific method to systematically improve. No matter where a group starts, iterative application of the scientific method, informed by comparisons with other professional groups, will eventually lead to documented best patient care. But without consistent care delivery practices it is not even possible to accurately measure outcomes, let alone systematically improve.

The costs associated with a health care process are just one more outcome of the process. As such, process management techniques apply to them just as well as to medical outcomes. This is the basis for the widely held but unproven view that efforts to eliminate variation will produce less costly as well as better care.

In an increasingly competitive medical marketplace, it is critically important to physicians and hospitals that they are able to *document* effective, efficient patient care, improve both quality and cost over time, and share the results with patients, purchasers, and regulators. In a very real sense, within a provider-at-risk environment a provider's financial success is tied directly to the provider's professional success. Both depend upon the provider's ability to measure and manage variation.

Lesson 3: For most physicians, financial rewards are secondary to good patient care. For that reason practice management efforts that emphasize patient care quality are much more successful, even for managing costs, than those that focus on costs alone.

The foregoing list of major sources of physician practice variation overlooks one oft-cited factor: Financial incentives clearly affect medical decision making (Wennberg, Barnes, and Zubkoff 1982; Eddy 1984; Hillman et al. 1992; Mitchell and Scott 1992; Mitchell and Sunshine 1992; Swedlow et al. 1992). But financial incentives exist within the broader context of professional uncertainty. When forced to choose between good patient outcomes (as supported by credible clinical data) and their own financial gain, most physicians consistently elect to maximize patient outcomes (consider, for example, Maine's experience with falling surgical rates following publication of outcomes data (Caper 1991)). More than that, physicians almost exclusively use the language of quality when they argue practice issues among themselves. Even financial arguments are usually couched in quality terms (Wennberg et al. 1977). By concentrating on quality of care (at the level of professional uncertainty) process management can align the moral weight of the entire medical profession with its goals, and control the context within which financial decisions take place.

Physicians' response to financial incentives may arise partly from nonphysicians' fixation on costs: Many practicing physicians perceive that health care administrators, regulators, and payers care *only* about reducing costs. If an administrator's ill-considered cost control efforts damage patient care, the patient and the physician are left to face the ethical and legal consequences alone. But as quality improvement theory (and related experience) clearly demonstrates, quality controls costs. One of the best ways to control costs is to manage quality. One of the biggest hurdles IHC faced in implementing clinical process management (in order to improve both quality and costs) was overcoming the distrust that years of monomaniacal cost control efforts had built among physicians. As IHC's administration

has shifted its emphasis to best patient outcomes (with secondary cost control in a quality improvement setting) physicians' willingness to collaborate on clinical process management has steadily increased.

Lesson 4: Guidelines are nothing new to American medicine.

When the LDS Hospital research team began to develop a protocol to control ventilator management for ARDS patients, they followed models that have seen continuous use in American medicine since the early 1900s. Physicians routinely use guidelines in daily practice (even though they often apply them subjectively) because it helps them deal with complex decisions and makes them more efficient (guidelines save time, as the LDS Hospital ARDS team so clearly demonstrated). As an extreme example, residents and interns routinely purchase, carry, and rely on books of medical guidelines specifically designed to quickly summarize the diagnosis and treatment of common conditions.

Lesson 5: "Control" is a central issue.

Why, then, would physicians resist the implementation of practice guidelines at a hospital level? One major reason is that they fear a loss of control. They see hospital-level practice guidelines as straitjackets that mandate decisions, fail to recognize the full complexity of real patient care, and eliminate clinical judgement. More than that, they perceive that control is wrested from them only so that administrators can control costs. The responsibility for bad patient outcomes still rests with the physicians, even after their control over patient care (and, hence, patient outcomes) is gone.

In contrast, medicine's traditional guidelines are decision support tools that recognize the need for clinical judgement. The LDS Hospital ARDS team addressed this issue by giving the clinical team control over the guideline. The use of statistical process control to measure guideline compliance, which inherently recognizes a range of appropriate (random) variation while still preventing inappropriate (assignable) variation, reinforces the critical role of clinical judgment.

Lesson 6: Implementing process management requires a partnership between physicians and administrators.

The idea of continuous improvement/process management is a central tenet of the medical profession. Every physician, upon entering the practice of medicine, ethically commits to examine the treatments they give to patients and the outcomes they achieve, with an aim to

improve their treatments for future patients. In medical school and residency training every physician also forcefully learns that they cannot trust subjective data—objective information and evaluation are essential to good treatment decisions. But for some reason, when physicians leave training and enter the practice of medicine, they begin to evaluate their treatments and outcomes subjectively, in their heads. Because of that subjectivity their practices often resemble a series of small, unplanned, uncontrolled human experiments, based on the last journal article the physician had time to scan or the last drug representative who visited the clinic. Obviously, that kind of medical practice—the kind practiced by almost all American physicians—has no chance of generating viable information about best patient care.

The central question, then, is "Why?" If physicians know that objective information is critical to the practice of medicine, why do they base their practice of medicine on subjective evaluations? As we implemented clinical process management within IHC, we had the opportunity to ask that question of many community-based and academic physicians, as well as examine its meaning in our own medical practices. We concluded that practicing physicians do not have the resources, the time, or the training to deal with the masses of data required for objective practice management. But data management is a well-established ability within health care organizations.

Effective guideline implementation requires a partnership. Physicians, working as a peer group, supply clinical leadership. They have the clinical understanding necessary to oversee the content and direction of clinical guidelines. They can meet (as a group) to discuss best patient care and to review guideline compliance. The hospital supplies staff support. Hospital staff collect, collate, and analyze the clinical data, and support the generation and maintenance of other guideline-related documents (such as flow charts).

Lesson 7: Local consensus is essential for implementing guidelines.

Because most clinical practices have no firm basis in published scientific research, those who generate practice guidelines are often forced to rely on expert consensus to complete their work. But even when generated through formal methods, expert consensus is an inexact tool. Different consensus groups have different goals and use different techniques. They often generate different, even conflicting, guidelines on the same topic (Kellie and Kelly 1991; Audet, Greenfield, and Field 1990; Leap et al. 1992). Within a single consensus panel the experts often disagree, and their assessments change when they apply guidelines generated in a theoretical setting to real patients (Park et al.

1989). Perhaps most troubling, physician experts show wide disagreements when asked to assess underlying probabilities that are essential to consensus judgments (Eddy 1984; O'Conner 1988). For example, Eddy (1992) asked thoracic surgeons, sponsored by a professional society, to assess the chance of a particular outcome for a well-defined group of patients within a specific time period after surgery. The outcome was an essential element to determine when the procedure was appropriate. The surgeons' assessments ranged from zero to 100 percent. In light of many similar examples, there is real doubt that such a thing as a "medical expert" truly exists.

As the LDS Hospital ARDS team recognized, expert consensus suffers from the same deficiency that produces practice variation in the first place: There are no data to show that consensus guidelines are correct. In such a setting, if the aim is to stabilize a care process then systematically improve, local consensus among the complete care delivery group is far more important than the consensus of an expert panel. An expert consensus panel can provide a jumping off point, to get a practice guideline started. But that expert consensus must translate into local consensus if the guideline is to modify physician practices.

Lesson 8: Effective guidelines require feedback on compliance and outcomes, using credible clinical data.

In 1989, Lomas et al. tracked the implementation of a practice guideline covering repeat cesarean sections in Canada. The guideline was developed and widely distributed by the major professional society that represented obstetricians in the country. In a survey, 87 to 94 percent of obstetricians told Lomas that they "agreed with the content" of the guideline; 33 percent said that, as a result of the guideline, they had changed their practice of medicine. But in a follow-up test only 67 percent of the obstetricians in the survey understood the guideline's contents. The actual repeat C-section rate was 15 to 49 percent above the rate reported by the obstetricians. Lomas concluded that the guideline had produced only "slight change in actual practice." Other investigators, upon evaluating the impact of dissemination for other guidelines, have found similar results (Kosecoff et al. 1987; Merz 1991; Cohen et al. 1992).

The LDS Hospital ARDS team generated data through which members of the team could objectively evaluate their performance against the guideline. In the face of credible clinical data, in a supportive environment, guideline compliance changed. Several other projects within IHC have shown the same effect, and other investigators have reported similar results (Caper 1991).

Subjective data works no better for guideline implementation than for care delivery. Successful guideline implementation appears to rest upon the availability of an adequate data system. But such a data system serves many other concurrent purposes in addition to helping establish guideline compliance. It provides information to assess outcomes and systematically improve, and generates reports for use with regulators and health care purchasers.

Lesson 9: Physicians will lead guideline implementation if the subject is approached through existing professional values, structures, and realities.

The values and standards of the American medical profession are a ready foundation upon which a successful guideline implementation program can securely rest. But to take advantage of that foundation, administrators must approach guideline implementation from the medical perspective, using structures and language that physicians understand. For example, physicians already have a structure to implement clinical management. It's called the medical staff. Therefore, as the LDS pulmonary research team began to implement their ventilator guideline, they did not add another layer of meetings. Instead, they used their existing clinical staff meetings. Similarly, time is a limited commodity for most practicing physicians. Asking community physicians to attend team meetings, outside of their existing quality structure, is tantamount to asking hospital employees to attend quality team meetings without compensation outside of regular work hours. At IHC, we therefore involve physicians in a supervisory role. Hospital employees invest the hours of staff work necessary to implement a guideline, regularly contacting physician leaders for oversight, direction, and approval. We call meetings of the entire subspecialty medical staff only after the staff work for a guideline or practice analysis is well advanced, and after physician leadership has already had a chance to review and criticize it.

CONCLUSION

In 1989 Linder interviewed 104 clinical and administrative leaders at 31 hospitals in the United States. All 31 hospitals used a large commercial severity-of-illness measurement system to compare the health outcomes achieved by individual physicians. All claimed to use the system as part of a quality improvement effort. But Linder concluded that 45 percent of the hospitals in the study used these tools primarily

to avoid meaningful change. Their outcomes measurement and quality improvement programs were a facade, a barrier to deflect outside criticism while they practiced "business as usual" behind their shield. For an additional 35 percent, the hospital administration used outcomes measurement and quality improvement to exert control over physicians. Only 20 percent of the hospitals surveyed used their systems to manage care processes—to build a partnership with physicians, and manage quality and cost through an informed and open discussion of difficult medical issues.

Linder's findings underscore a central issue in guideline development and implementation. Because most medical decisions have no basis in published scientific research, consensus techniques are essential to build practice guidelines. But for a significant subgroup of health care leaders, some opinions are more valuable than others. On one side is a group of "experts" (members of the guideline development team) who can think, while on the other side (practicing clinicians) are those who can only do what they are told.

A group of "experts" can generate a practice guideline. A hospital administration can mandate that practicing physicians follow its rules. But given the realities surrounding the science of medicine, consensus methods, and the practice of medicine, effective implementation will occur only when clinicians and administrators team together to find the best patient care. That union is the sole safe haven in an increasingly competitive provider-at-risk environment. It not only creates the means to manage costs and improve patient outcomes; it generates the information necessary to market effective, efficient care to purchasers.

For the next generation of American health care systems, success will depend on the ability of health care leaders to create a culture of cooperation among all members of the health care team. Those leaders will not manage physicians. Instead, they will organize clinicians then supply them with the necessary tools, so that physicians can manage themselves and the health care processes they oversee. In creating that collaborative culture, it is obviously far more important how health care leaders implement practice guidelines, than the particular set of guidelines that they use to initiate implementation.

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Testimony of Barry Marshall, M.D.

**Before The Subcommittee on Regulation,
Business Opportunities And Technology**

October 21, 1993

My name is Barry Marshall, I am a Medical Practitioner trained in Perth Western Australia and also qualified as an internist in the United States. I am a permanent resident of the United States and have lived in Charlottesville, Virginia since 1986. I am an Associate Professor of Medicine at the University of Virginia in Charlottesville.

In the year I left Medical School in Australia, I observed the introduction of the Australian comprehensive health scheme modeled on the Canadian system. That plan allowed completely free unlimited access to health care. It was overutilized by patients who no longer saw the value of what became a free government service. Very quickly the system became too expensive and so financial constraints were used to limit access to expensive new drugs and technologies. Whenever possible, patients carried extra health insurance so that they could have a better choice of doctor and could obtain more convenient access to improved health services. I believe that about 40% of Australians are privately insured, even though, if they elect to, they can obtain completely free care at a government hospital.

The best aspects of the Australian system seem to be embraced by the new U.S. system i.e. universal basic coverage. This type health plan allows Australians to live a rather carefree life with no need for long term individual health planning. Immunization and public health planning ensure that most Australians are healthy. The expense of catastrophic illness is of no concern so there is less pressure towards litigation by persons with bad health outcomes.

The Australian system ran over budget I believe, because it was completely free to the general public. There was no co-payment and medication costs were heavily subsidized The actual cost and value of such a free service was not appreciated by patients. In addition, since there was no value set on the services provided, there was no way one could measure new or more efficient use of health services. Nowadays, about 40% of Australians keep private insurance because it provides more choice and is more convenient than the public system.

The down side of the Australian system is that it competes with and stifles private industry. The profit margin for diagnostic products in Australia is low. Scientists in public hospitals can manufacture competing diagnostic products *for a few cents* (no estimate of overhead is necessary). Therefore,

entrepreneurs do not see any benefit in developing new products which might ultimately be manufactured more efficiently, marketed properly, and subsequently exported. My own example is a small diagnostic test I patented. The test costs $6.00 and replaces a pathology fee of at least $150.00. The test is a good value and sells more than 100,000 per year in the United States. In Australia sales are low because the new test costs US$3.00 whereas the competing pathology service does not generate a bill for the patient and is therefore seen to be free. In addition, hospital laboratories in Australia infringe the patent, manufacture the test *for a few cents* and never account for their overhead costs as the manufacturer must do.

BRIEF DESCRIPTION OF CLINICAL STUDIES COMPARING ALTERNATIVE TREATMENT TECHNOLOGIES FOR GASTRIC AND DUODENAL ULCERS:

PEPTIC ULCER: OLD DOGMA

Peptic ulcers affect about one in ten persons, about 4 million people currently either have gastric (stomach) or duodenal peptic ulcers and at least that many persons take acid reducing medication each day to prevent ulcer attacks. Typically, peptic ulcers (ulcers exposed to acid) are shallow holes in the lining of the stomach or adjacent intestine. They come and go during life, sometimes causing severe, or even fatal, internal bleeding. Until recently, the only cure of ulcer disease was by stomach surgery. Most ulcer patients experience a recurrence of their ulcer within a few months of stopping their medication. Many ulcer patients must take medication continuously, costing about $50.00 per month. The medications commonly used are called H2-blockers and have brand names such as Tagament, Zantac, Axid and Pepcid. I believe that sales of these drugs total about $2B per year in the United States, half being used by ulcer patients. In addition, ulcer patients often require expensive investigations such as upper G.I. series ($2-400) and endoscopy ($4-800).

Because the cause of peptic ulcer was unknown, many people blamed stress, bad diet, alcohol and cigarette smoking. We now know these factors are mostly irrelevant.

THE DISCOVERY OF HELICOBACTER "ULCER BACTERIA"

In 1982, I discovered that nearly all persons with duodenal ulcers or gastric ulcers were infected with previously undiscovered helical or spiral bacteria which we now call *Helicobacter pylori* (or *H-pylori* for short).

The new bacteria infected the lining of the stomach and caused inflammation known as gastritis. It was known that gastritis was present in nearly all persons with so-called peptic ulcers. I proposed that gastritis was the underlying cause of

peptic ulcer. If the bacterial infection could be cured, then the gastritis would heal and the ulcers would be permanently cured.

NEW THERAPY:

In 1984, I discovered that the *H.pylori* could be cured with a 14 day treatment consisting of bismuth (a similar compound is in Pepto-Bismol) plus an antibiotic. The cost of this treatment was about $40.00. Since then an improved version with 2 antibiotics and Pepto-Bismol has been shown to give an 85% cure rate and costs $42.00.

From 1985 to 1987 I conducted a double blind trial in Australia. I showed an 85% cure of peptic ulcer for patients who were cured of the bacterium.

I presented my initial double-blind study at the American Gastroenterological Association meeting in May 1987. The paper was published in the Lancet in December 1988. In other countries, including the United States, researchers were able to duplicate my work, all showing cure of ulcers after eradication of *Helicobacter pylori*. Several papers have now described cure of duodenal ulcer after this kind of treatment.

TWO STRATEGIES FOR GASTRIC AND DUODENAL ULCERS:

The old strategy is to ignore the presence of *H.pylori* and to treat the patient with H2-blocker drugs at a cost of about $600 per year. After an initial 4-6 week treatment to heal the ulcer, the patient may cease the drugs (and wait for his ulcer to recur) or may continue to take it in half dosage to protect from the ulcer.

Many doctors do not even test for an ulcer. They just give the drugs and presume that it must have been an ulcer is symptoms improve.

The new strategy is to test the patient for *H.pylori* when he/she develops ulcer symptoms. If *H.pylori* is present, then antibiotics may be prescribed as well as H2-blockers. In this way, most patients only need to be treated once in their lifetime. They probably do not transmit the *H.pylori* to their children, and the so-called hereditary diseases of peptic ulcer is permanently cured.

Currently, some doctors recommend that only patients with ulcers receive treatment for H.pylori. In other words, after finding *H.pylori*, doctors must then detect an ulcer as well before treatment starts. This means that the expensive investigation mentioned above must still be done.

Alternatively, if *H.pylori* is present and symptoms are compatible with an ulcer, doctors might just treat the *H.pylori* in any case. Thus if an ulcer was present it would be cured. If an ulcer was not present then the *H.pylori* would be cured and the patient would be protected from developing an ulcer in the future (1% risk per annum.)

DIFFERENCE IN CLINICAL OUTCOMES

With the old treatment, the ulcer is not cured and tends to recur. Patients must continuously take medication to prevent this happening.

With the new treatment the ulcer is cured. Suddenly peptic ulcer is a simple disease just like strep-throat, a bladder infection or sinusitis. It does not need to be feared, no life-style modifications are necessary, and patients need not puzzle over the often overrated component of stress.

WHY?

For many years it was known that most patients with peptic ulcer produced an excess of stomach acid. We know now that *H.pylori* causes gastritis which leads to increased acid production. The stomach does not turn itself off completely between meals. After *H.pylori* is cured, acid production returns to normal in most persons.

WHO HAS H.PYLORI?

H. pylori is mainly a disease of older persons (who caught the germ in childhood), minorities and lower socioeconomic groups. African Americans, Latin Americans, Asians and immigrants from Eastern Europe have an infection rate of 40-80%. These are the people who have ulcers now, and who will develop peptic ulcers in the future.

Persons with *Helicobacter pylori* also run a small risk (1%) of developing gastric cancer.

WHAT IS THE DIFFERENCE IN COST?

The table below shows estimated cost and cost saving per year for patients treated the old way (H2-blockers) versus the new way (antibiotics).

See MD; diagnose ulcer	Therapy of ulcer for 2 mo	Therapy for rest of year 1	Therapy year 2-5	5 year Cost	Cost for 4 million people	Savings over 5 years
$75+$500	$75+$75	$525	$2000	$3250	$12.2B	
See MD; diagnose *H.pylori*	Therapy of *H.pylori* and ulcer for month	No therapy required	No therapy	No therapy		
$75+$100	$75+$100	$0	$0	$350	$1.4B ($2.8)	$10.8B ($9.4)

The table does not account for *Helicobacter pylori* treatments in patients who did not really have an ulcer (double costs in H.pylori row shown in parenthesis.) Table does not take into account pain, suffering and other costs of ulcer diseases (costs in upper row could be double).

WHAT EFFORTS DO YOU ANTICIPATE WILL BE MADE TO PROMULGATE THE DISCOVERY ACROSS THE U.S. AND ELSEWHERE?

The drugs used for treating *H.pylori* vary from generic combinations ($42) which are less convenient, to proprietary combinations ($100-$200) which are easy to take for the patients. The generic cheaper type has been available and has been known for about four years. It was never submitted to the FDA because it would have cost at least $50m to evaluate such a three drug therapy to their usual standard. Profit margins would have been low because these were generic and over-the-counter drugs. If evaluation had begun in 1989 then we may have had that medication in the market now. Unfortunately, because this therapy was so cheap, it could never see the light of day in the United States.

The very new anti *H.pylori* therapies using proton-pump inhibitors and one or two proprietary antibiotic are about the same effectiveness as the treatment mentioned above. Patients have cure with little inconvenience and few side effects. Even though these therapies are expensive, they are only give once. Therefore, there is a very large saving over the old type of acid reducing treatment which required continuous or repeated administration.

Because these new therapies are given only once, they do not produce the recurring profits which were once seen with the old H2-blockers. Therefore drug companies will not invest as much into research for their use.

NEW DRUGS UNDERGO RIGOROUS TESTING; HOW WOULD YOU ASSESS THE ADEQUACY OF INFORMATION FROM THESE TRIALS AS THE BASIS FOR DECISION MAKING BY CLINICIANS, PATIENTS AND PAYERS?

The U.S. has the highest standard in the world for the approval of new drugs. Perhaps because of the litigation here, mistakes in early approval are far more likely to have severe consequences for drug companies and the Government (or Government employees) who make them.

New drugs are tested in very selected groups of patients. Sometimes these selected groups do not reflect real life. New study designs should encompass large groups of patients in real life situations. To make this affordable, the FDA may have to be cost conscious and assess the risk-benefit of its very tight standards. For example, after initial evaluation, some studies could be done in primary care setting with remote monitoring by mail, telephone calls and less frequent doctor visits. This type of approach may be appropriate when drugs have already been evaluated and used in other countries.

In the case of Pepto-Bismol and antibiotic therapy, such a plan would be easily implemented. In fact, the therapy has been evaluated in the United States but has no sponsor for passage through the FDA.

Most MD's and drug company personnel (myself included) are very hesitant to criticize the FDA. a confrontational attitude towards such a powerful government agency could easily cost millions of dollars.

LEADING HEALTH REFORM PROPOSALS WOULD FACE TREMENDOUS FINANCIAL PRESSURE ON PAYERS TO CONTROL HEALTH CARE PRICES AND UTILIZATION, LEADING TO CONCERNS ABOUT COVERT, UNACCOUNTABLE HEALTH RATIONING. CAN THESE CONCERNS BE ADDRESSED THOUGH IMPROVEMENTS IN THE SCIENTIFIC INFORMATION SUPPORTING DECISIONS BY PAYERS, PATIENTS AND PRACTITIONERS IN THE HEALTH CARE MARKET?

At present there is apparently no incentive for large health care concerns to find new ways of saving money. I approached Blue Cross Virginia in 1987 but they told me that they did not support funded research. Although new technology is often very cost effective, there may be no incentive to introduce it. For example: if my insurance always reimbursed $500 for an ulcer patient, which manager would risk the expense of finding a better cheaper treatment? On the other hand, if Blue Cross could treat an ulcer patient for $250, the profit could be turned to new improved services for other patients.

HOW WERE YOUR STUDIES FUNDED? IN YOUR VIEW, IS THERE AN ADEQUATE AND STABLE SOURCE OF FUNDING FOR COMPARATIVE HEALTH CARE TECHNOLOGY ASSESSMENTS OF THE SORT YOU CONDUCTED?

My studies were funded initially by the Australian medical system which, because it does not raise any bills, allows research for free. Subsequently, I was funded by the Australian

NH&MRC, the equivalent of the NIH. After 1986, I was funded in the United States by the Proctor and Gamble Company, makers of Pepto-Bismol. P&G supported research into H.pylori and spent at least $10m over the years 1987-90. P&G owns the patents for bismuth treatment of ulcers.

Since 1990 many drug companies have shown interest in H.pylori and ulcers. These have supported research at many universities including the University of Virginia. Other researchers have received research grants from the NIH. Compared to other funding, the NIH funding of H.pylori research has been meager. According to my information it has been less than $5m per year over the past six years (1987-93). With $1B return at stake this seems inappropriate.

Testimony of Eric J. Topol, M.D.

Before the Subcommittee on Regulation, Business Opportunity and Technology

October 21, 1993

The importance for randomized, controlled, trials in medicine cannot be adequately emphasized. Such trials provide the best validation of a particular therapy -- be it a new device or pharmaceutical intervention -- and are powerful scientific tools, a yardstick for assessing the true benefit, risk and cost of new procedures and treatments. While well conducted trials are widely recognized as being valuable to clinical-decision making and can have a major impact on the daily practice of medicine, there is substantial dearth of clinical trial data available. This is especially the case with new medical devices.

The history of medical practice provides multiple examples of well-intentioned clinicians applying therapies to patients in the absence of controlled proof of efficacy from clinical trials with disastrous results. Some of the more well-publicized examples include gastric freezing for stomach ulcers and the use of pericardial debridement for coronary disease. Even in the 1980's the use of drugs to suppress asymptomatic arrhythmias was widespread until controlled trials showed that these drugs increased the risk of death. The reason that these errors in judgement were made by highly intelligent and motivated clinicians is that the application of medical therapies to patients with complex diseases is so difficult to interpret that except in rare circumstances, the only way to be sure that the results are not the results of bias is to perform a randomized trial. These trials are time consuming and expensive, and they require the physicians and the manufacturers to state in plain English that the value of the procedure is unknown, and that is why it must be tested. In our current system, there is every disincentive for the performance of clinical trials.

In participating with the Agency for Health Care Policy and Research (AHCPR) for preparation of Guidelines in clinical medicine, it has become remarkably clear how frequently we do not have sufficient data from rigorous trials in order to make appropriate recommendations. Instead, the process largely relies on the opinions of an expert panel, which can be particularly subjective and are often proven wrong at a later date. Therefore, for future ability of clinicians to make informed decisions and for establishing meaningful Practice Guidelines, maximal facilitation of prospective, randomized trials would be a pivotal goal.

Recently, we had the opportunity to perform a large, randomized, multicenter trial of a new coronary artery device known

as atherectomy, which is a technique in which the atherosclerotic cholesterol blockage (plaque) is removed with a catheter. This procedure was introduced for investigational use in October 1986 and approved by the Food and Drug Administration in September 1990 for commercialization. During the first calendar year after approval in 1991, 17,000 procedures were performed at an equipment cost exceeding $35 million. The rapid acceptance of the new technique, despite the lack of data from a randomized trial, was largely a reflection of the new ability to actively remove plaque rather than simple stretching the arterial channel with a balloon. In 1992, more than 33,000 procedures were performed in the United States and it is projected that more than 60,000 will be performed this year.

The accepted standard technique for non-surgical treatment of coronary artery narrowing is balloon dilation, known as angioplasty. We compared the two techniques, atherectomy versus angioplasty in 1,012 patients in 35 hospitals from the United States and Europe, for outcomes (cumulative to 6 months) and cost. The project is known as the Coronary Angioplasty Versus Excisional Atherectomy (CAVEAT). Our findings were reported in the New England Journal of Medicine (329:221-7, 1993). The entire cost of the randomized trial was less than $2.3 million and the recruitment was rapidly completed in only 7 months. This was the largest trial of a new medical device ever performed. The following Table summarizes the key results:

Primary CAVEAT Findings:

	Death	MI*	Need for Repeat Procedures	Cost**
Atherectomy	1.6%	7.6%	36.5%	$11,904
Angioplasty	0.6%	4.4%	37.2%	$10,637

MI = heart attack, *P = 0.04, **P = 0.006

Thus, we found that atherectomy, the new technique that is unique in its ability to actually remove the plaque, had more complications, cost more ($1300 per case), and did not achieve its objective of reducing the number of repeat procedures during follow-up. While atherectomy is an important advance and still quite useful for select patients, these data indicate that until the procedure is improved, it is not suitable for wide application.

This also demonstrates that a new technology can be quickly

assessed and that the results may be quite different than what were anticipated. In the case of atherectomy, the cardiology community fully expected there to be a significant edge for the innovation. Within 1 year of FDA approval, the trial had been initiated and the results available only two years from the time the device was commercially approved. Of note, such a large effort could not have been executed before the Pre-marketing Application Approval (PMAA), owing the need for a critical number of participating sites with adequate technique experience. It is therefore recommended that there be consideration for provisional FDA approval of devices, contingent on the prompt completion of a randomized clinical trial.

Having precise data for a new technology is of immense value to all parties concerned - physicians and hospitals, the payors, and the device or pharmaceutical manufacturers. In the example of atherectomy, by defining the procedure was not, at this point, a clearcut advance, hypothetical reduction of the annual number of procedures from 60,000 (15% of all non-surgical interventions in the United States) to 20,000 (5% of procedures) would result in an over $50 million savings each year. This trial has also stimulated the device manufacturer and cardiologists to continue toward improving the technique. Many innovations will yield improved outcomes and lower costs; it is imperative that the data which proves these findings becomes available in a timely manner.

The Government should consider providing special incentives to promote well-conducted, randomized trials of new technology. These trials can be a significant expense for a small company, such that collaborative sponsorship from payors (including governmental sources), who stand to gain considerably from having the data, be strongly considered. Sponsorship of trials represents a significant obstacle to their successful completion. Unfortunately, there is virtually no support for such trials from the National Institutes of Health or other independent agencies, and marked unfamiliarity of small companies with trials, including unwillingness to have the projects completed in a fully independent manner (by the academic community). These are further deterrents for high quality, comprehensive clinical research projects.

The incentives of extended exclusivity and expedited approvals are quite reasonable methods to further promote the interest of companies to proceed with a trial. Currently, the FDA does not consider the cost-related issues in the approval process of a new technology and the AHCPR is not involved with the approval of new technologies outside of promoting Practice Guidelines or sponsorship of independent research projects. Thus, setting up incentives and appropriate structure to review the design and findings of randomized trials will help affect meaningful progress in an area of medicine that desperately need improvement. In such a way, the mutual goals of promoting innovative technologies and cost-containment may be achieved.

United States House of Representatives
Committee on Small Business
Subcommittee on Regulation,
Business Opportunities, and Technology

STATEMENT ON WYDEN PROPOSAL FOR PRUDENT PURCHASING AND USE OF MEDICAL TECHNOLOGY

18 Oct 93

Statement by John W. Williamson, M.D.
Director of Salt Lake RMEC, Dept. of Veterans Affairs
Professor of Medicine & Professor of Medical Informatics
University of Utah School of Medicine

Mr. Chairman, distinguished members of the Subcommittee.
It is an honor and a pleasure to provide this statement regarding this important proposal of Congressman Ron Wyden.

I have been a physician and an academic researcher - a Professor at Johns Hopkins nearly 19 years, a visiting Professor at Harvard for 2 years, and most recently a Professor at the University of Utah School of Medicine for 9 years. During this 30 years I have focused my career on two themes: first, health care quality assurance, and second health science information management, both directly involving medical technology assessment. Recently I have been privileged to be a member of the Interagency Task Force for Health Care Reform, headed by Hillary Rodham Clinton. (See **Attachment A** for a more complete listing of my credentials.)

I, and trusted colleagues I have contacted*, judge that the Chairman's proposal for prudent purchasing of drugs and devices by use of comparative medical technology assessments, is both urgent and critical. If implemented it could make a major contribution in reducing health care costs, and improving care quality. However, generating valid technology assessment data is difficult, and even when available, it may take up to 10 or 15 years to be applied widely, as pointed out by

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* Frederick Mosteller, who with Thomas Chalmers, heads the Health Technology Assessment Division of the Department of Health Policy and Management at the Harvard School of Public Health; Stanley J. Reiser, M.D., Ph.D., Co-Editor of the International Journal of Technology Assessment in Health Care; Peter Goldschmidt, M.D., D.Sc., Director of World Development, Inc., a consultant to the Institute of Medicine, who has conducted technology assessments for over 25 years; Theodore Colton, Ph.D., an internationally recognized health statistician at the Boston Medical Center, long interested in health technology assessment.

Chalmers and others.[1, 2, 3, 4] In my testimony today, I would like to suggest three provisions that might make this important proposal even stronger:

1. Emphasize use of valid research guidelines to assure soundness of new comparative technology assessments generated;

2. Develop syntheses of existing studies to both strengthen new research and directly facilitate current purchasing;

3. Use computerized expert systems to assure rapid dissemination and appropriate use of the above information that is produced.

My first point is that there are clear advantages for encouraging manufacturers to generate new studies, not only for establishing product efficacy and safety, but also cost-effectiveness compared with current alternatives. This effort could be strengthened by use of valid research safeguards currently available from such renown investigators as Bailar and Mosteller [5] at Harvard, or Hillman [6] at Pennsylvania. For example Hillman states that pharmaceutic cost-effectiveness analyses sometimes tend to be "marketing devices" rather than sound clinical research.[6] Mills' cogent article in the New England Journal of Medicine [7] stated: "If you torture your data long enough, they will tell you whatever you want to hear." However, use of sound research guidelines could substantially reduce bias, and improve the value of the data produced.

My second point is that it is difficult to adequately identify, validate and synthesize, results from either new or old studies. [9, 10, 11] However, new methods now exist to alleviate this problem, [12] I would suggest incentives and funding for researchers, to apply these new methods to produce many additional information syntheses of existing studies on comparative medical technology. Unfortunately, most current published literature reviews are often not trustworthy, for lack of an adequate search strategy and use of appropriate validation of the information included. There is a profusion of literature from which these studies might be based. [13] Some estimate that up to 20,000 (extrapolated [13]) medical journals are published annually in the English language, with 3700 indexed in Medline.[14] The Cochrane Centre in England compiled over 15,000 clinical trials on pregnancy and child birth technology alone.[15] Excellent models of narrative syntheses are available as illustrated by Peterson's book, "Health Care of the Elderly,"[16] and the serial publication, "American College of Physicians Journal Club." [17] The bad news is that inadequate or sloppy literature reviews can be self-serving, allowing authors to falsely conclude there is no current information on the topic they propose to investigate.

My third suggestion would be for incentives and funding to improve dissemination of sound comparative technology assessments by using computerized expert systems. Haynes, at McMasters University, states: "Peer-reviewed journals impede the dissemination of validated advances." [11] When facing a patient, busy physicians will rarely read journal articles, or even available guidelines. Expert systems can apply the power of technology assessment studies in milliseconds while the physician is making his management decisions. Such systems are key to assuring timely and appropriate use of valid advances, particularly for drugs and devices.

To illustrate, recently a 40 year old patient experienced the classic symptoms of an acute heart attack. Emergency room clinicians sent him to a major cardiac center for care. Later that day, independent of official care, available findings were put into a desktop computer expert system called Iliad, [18, 19, 20, 21] which incorporates over 1600 medical guidelines. The results indicated a low probability of an acute myocardial infarction, with the highest probability being an esophageal spasm that could be easily treated with new proven pharmaceuticals. Ten weeks later, after a $12,000 workup, including coronary catheterization, the diagnosis of esophageal spasm was finally made. On the first day of the patients illness, the expert system had suggested the correct diagnosis that could easily have been confirmed by the physician asking a couple of simple questions. This information might have averted hospitalization, inappropriate use of expensive potentially life-threatening devices, and appropriate use of recently proven new pharmaceuticals.

Another example is an expert system developed for patient use. A middle aged male, who recently had nausea and vomiting, was asked to use this system to elicit his history while waiting for the doctor. This system asked the patient questions requiring simple yes or no answers. It then produced a printed history, together with the probabilities of the most likely diagnoses that would explain the patient's symptoms. Unfortunately, at that time the clinicians usually disregarded these printouts due to their pressured clinic schedule. The practitioner caring for this man, not reading the printout, diagnosed him as having gastroenteritis, and sent him out with a prescription for drugs. As the patient left, the clinician just happened to glance at the computer print-out. He then yelled at the nurse to get the patient back for an emergency hospital admission. The practitioner discovered from the printout that he had failed to ask the patient about the character of the vomitus. The expert system had asked this question and discovered that the vomitus had resembled coffee-grounds the day before and was bright red this morning. As the expert system suggested, this patient did not have simple gastroenteritis, but was hemorrhaging from an ulcer. Consequently use of new proven pharmaceuticals alone would have been

inappropriate. If only drug treatment had been given this patient, the outcome might have been tragic.

I suggest to the Subcommittee that incentives for use of research methods guidelines, together with incentives and funds for more rapid development of valid literature syntheses, incorporated into computerized expert systems, could have immediate and dramatic benefits. Overall, the Chairman's excellent proposal, augmented by these provisions, could result in substantial cost-savings and better health outcomes for the nation.

I thank you again for this opportunity to share these ideas with you.

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ATTACHMENT A

Professional Credentials of John W. Williamson, M.D.

I am a physician and academic researcher. I was a Professor at Johns Hopkins for nearly 19 years; a visiting Professor at Harvard for 2 years; and currently I am a professor of Medicine and a professor of Medical Informatics at the University of Utah School of Medicine.

For over 30 years I have focused my career on the field Quality Assurance / Quality Improvement of Health Care, and Health Science Information Management. Through my students, I provided input to the Bennett Amendment to the Social Security Act, that established Professional Standards Review Organizations (PSROs) to assure quality of care for Medicare and Medicaid patients. I worked directly with Paul Ellwood to write the quality assurance section of the HMO Act of 1973.

In 1966, I was one of the original faculty members of Dr. Kerr White's new Department at Johns Hopkins devoted to health services research. Our group was central to the founding of the National Center for HSR&D, later named Health Services Research and Technology Assessment, the direct forerunner of the current Agency for Health Care Policy and Research.

In the 1970's I did research in the field of health science information management, that encompasses identification of clinical science information needs; retrieving relevant and valid information to meet those needs; and finally facilitating use of that information to improve health care decisions by both providers and consumers of care. This field encompassed such science information as Health Care Technology Assessment, epidemiology, health economics, health care management, health care systems, and ethical-legal topics.

My 1035 page book on Improving Medical Practice and Health Care - A Bibliographic Guide to Information Management in Quality Assurance and Continuing Education was started in the late 1960's, and published in 1977. This work addressed the difficulties obtaining relevant and valid scientific information (e.g., technology assessments) for improving clinical decision-making. It provides a unique literature classification system for this purpose and 3500 abstracts of illustrative literature.

My work, with Dr. Peter Goldschmidt and Irene Jilson on the Medical Information Demonstration Project in the 1970's was directly sponsored by two successive Under-Secretaries (Drs. Theodore Cooper, and Julius Richmond) of the then Department of Health, Education, and Welfare. This work was accomplished with the direct collaboration of the Director of the National Institutes of Health (Dr. Donald Frederickson). This study suggested a serious paucity of both relevant and valid scientific information for improving quality and cost-effectiveness of health care. It provided a model to cope with this problem, based on structured group judgment of experts, building on whatever solid data that did exist.

In the late 1970's I was a consultant to the staff of then Representative Albert Gore, Jr. of Tennessee when he was on the Subcommittee for Science and Technology Oversight.

I was a consultant to Congressional Office of Technology Assessment, working with the Director Joyce Lashoff and her Deputy David Banta. Banta was the recent recipient of likely the first academic chair in Technology Assessment and currently works in the Netherlands in this international field of endeavor.

I was a consultant to the National Center for Health Statistics, being one of the original founders of the National Ambulatory Medical Care Survey which today will provide critical information for planning health care reform, particularly in the ambulatory arena.

I have published over 10 books and monographs, and over 100 papers on Health Care Quality Improvement and Health Science Information Management. One of my more recent articles on the latter topic was published in a peer reviewed journal edited at the Karolinska Institute, Stockholm, Sweden.

I have been a member of Workgroup 9 (Health Care Quality) of the Interagency Task Force for Health Care Reform, headed by Hillary Rodham Clinton

Statement by

Lawrence Friedman, M.D.
Director
Division of Epidemiology and Clinical Applications
National Heart, Lung, and Blood Institute

for the

Committee on Small Business

Subcommittee on Business Opportunities and Technology

United States House of Representatives

October 21, 1993

Mr. Chairman and members of the subcommittee, I am Dr. Lawrence Friedman, Director of the Division of Epidemiology and Clinical Applications, of the National Heart, Lung, and Blood Institute (NHLBI). Thank you for this opportunity to provide testimony on the scientific evaluation of medical therapies.

Potential medical therapies can be evaluated in various ways. One scientifically well-accepted method is the randomized clinical trial, in which one or more therapies are compared. Patient participants are randomly assigned to the therapies, then followed over time to observe how they respond. Several medically important questions can be answered by a randomized clinical trial:

* Is the promising new therapy better than the existing standard therapy?
* Is the new therapy at least as good as an existing standard therapy? If so, does it have fewer adverse effects, or is it less expensive or easier to administer?
* If no accepted standard therapy exists, is the new therapy better than no therapy? In this case, the new therapy is commonly compared against an inactive substance, or placebo.

Often, physiologic or biochemical measures such as blood pressure or serum cholesterol are considered when evaluating a new

therapy. However, the effect of a therapy on these measures may -- or may not -- translate into a meaningful effect on the health of patients. For instance, many clinical trials have shown that reducing blood pressure can have a beneficial effect on outcomes such as stroke, and that reducing cholesterol can have a beneficial effect on coronary heart disease. However, other trials have failed to demonstrate the benefits of modifying a physiologic or biochemical measure. The National Heart, Lung, and Blood Institute's Cardiac Arrhythmia Suppression Trial (CAST), discussed below, is an excellent example.

Sudden cardiac death is a major public health problem. It is estimated that 250,000 people have sudden cardiac death each year in the United States. Also, it has long been recognized that cardiac arrhythmias, particularly those arising in the left ventricle, are strongly related to sudden cardiac death. In consequence, many scientists and physicians therefore concluded that it made sense to treat these ventricular arrhythmias.

There are various sorts of ventricular arrhythmias, and some are far more serious than others. The most serious ones are immediately life-threatening, and even the less serious ones are associated with increased risk of sudden cardiac death. It is a prudent, and indeed common, practice to treat patients with serious arrhythmias, despite lack of definitive proof that antiarrhythmic drugs or devices prolong survival. It is

considered sufficient that the drugs and devices either abolish the arrhythmia or convert it to a normal heart beat. However, many doctors (perhaps 50 percent of cardiologists, according to a survey) have also treated less serious arrhythmias, on the assumption they were preventing sudden cardiac death. The largest group of such patients includes those who have suffered a heart attack, many of whom have mild to moderate arrhythmias.

CAST began in 1987. Its purpose was to compare the safety and efficacy of three drugs that had been shown to reduce arrhythmias, and to determine if these drugs reduced the incidence of sudden cardiac death in heart attack survivors with mild to moderate ventricular arrhythmias. The drugs were compared against a placebo.

Two of the three drugs, encainide and flecainide, were widely used. Together, they accounted for an estimated 600,000 prescriptions in the United States in 1987, and almost 800,000 in 1988. In 1989, between 200,000 and 400,000 patients in the United States were on either encainide and flecainide. The third drug, moricizine, was not approved by the Food and Drug Administration (FDA) until 1990.

In 1989, CAST found that encainide and flecainide not only did not help the patients, but in fact harmed them, leading to a two- to three-fold increase in sudden cardiac death and all-cause

mortality. In 1991, moricizine was also found to be harmful when initially given, and not helpful when given long-term.

As a result of CAST, the FDA modified its guidelines for use of antiarrhythmic drugs, tightening the recommended indications, but not necessarily requiring the conduct of clinical trials with clinical outcomes before approving new drugs.

Based on physician surveys, clinical practice appears to have changed, with fewer physicians prescribing drugs of the sort studied in CAST for the kinds of patients studied in CAST. However, it appears that other antiarrhythmic drugs are being prescribed as frequently as before, and perhaps more frequently, to make up for the reduction in prescriptions of CAST drugs. The continued use of other antiarrhythmic drugs for patients similar to those in CAST may reflect a problem of education of physicians, given the fact that cardiologists tend to prescribe the drugs less often than general practioners.

Some implications of CAST are:

1) Often, only sufficiently large clinical trials with defined clinical outcomes can give answers about the efficacy and safety of medical treatments.
2) Use of physiologic or biochemical measures, so-called "surrogate outcomes," may be misleading.

3) Dissemination and incorporation of trial results into clinical practice may require considerable effort.

4) Although not proven, it is likely that other antiarrhythmic drugs have effects similar to those found in CAST. It is impossible to evaluate all such drugs definitively, and therefore reasonable judgments must be made.

It is important to emphasize that therapies that may be harmful in one setting may be beneficial in others. Though encainide, flecainide, and moricizine were harmful to the CAST patients, who had mild to moderate arrhythmias, this does not mean the drugs may not be beneficial to patients with more serious or immediately life-threatening arrhythmias. These drugs have not been adequately evaluated in serious or life-threatening cases. However, because of the high mortality rate in such patients, it may be reasonable to accept such uncertainty and treat them using best judgment.

American Medical Association
Physicians dedicated to the health of America

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November 15, 1993

The Honorable Ron Wyden
Subcommittee on Regulation,
Business Opportunities and Technology
Committee on Small Business
U.S. House of Representatives
B-363 Rayburn House Office Building
Washington, DC 20515

Re: The Cost of Medical Technology

Dear Chairman Wyden:

The American Medical Association (AMA) respectfully asks that these comments be included in the record of the October 21, 1993 hearing of the Subcommittee on Regulation, Business Opportunities and Technology of the Small Business Committee on the cost of medical technology in our Nation's health system.

Research shows that three major factors account for most of the growth in health care expenditures -- general inflation, increases in and the aging of the population, and innovations in health care technology. During the past thirty years, medical technology has played a direct role in major improvements in the health status of the average American. However, the increase in longevity and improved quality of life are not without an economic cost, and this increasingly is a matter of concern. In our support for health system reform, we hope to see expanded access to medical care and its technological advances. As a Nation and for its citizens, we cannot afford to stifle medical research and technological innovations.

The impact of new technology on aggregate health care expenditures is not well understood. Estimates of how much medical technology adds to total US health care spending have ranged from 10 to 40 percent. (The appendix attached to this letter provides some specific insights into the role and cost of health care technology in America.) The Prospective Payment Assessment Commission, in a June 1992 report to Congress, estimated that increased intensity of services provided for the following percentages of growth in health care spending from 1985 to 1990:

- 41.4 percent of the increase in the cost of inpatient services;
- 30.6 percent of the increase in the cost of outpatient services;
- 37.5 percent of the increase in the cost of physician services; and
- 32.6 percent of the increase in the cost of nursing home services.

(While it is not possible to attribute all of the elements that make up "increased intensity" to technological advances, there is no disputing that technological abilities are a significant factor in the intensity of care.)

Physicians can look at individual benefits from technological advances, but little is understood about the **net** effect that technologies have on the system as a whole. We know that innovative medical technology helps people live healthier, longer lives. We know that it can improve the quality of care that physicians provide. We know that, when it is our patients and their loved ones who are sick and in need of medical treatment, they want only the latest, most advanced medical care available.

Few of us would act any differently, as the positive effects of technological advances related to health care are enormous. For example:

- reducing pain -- the latest non-steroidal anti-inflammatory drugs relieve the pain, swelling and stiffness of arthritis, enabling millions of older people to lead more active lives;
- shortening recovery periods -- surgeons now increasingly can use a laparoscope for operations, such as a cholecystectomy, requiring only a very small incision and dramatically shortening the recovery period;
- improving functional outcomes -- orthopedic devices have restored function to patients who previously had been incapacitated by advanced arthritis, fractures, and bone disorders;
- allowing earlier diagnosis -- mammograms allow earlier diagnosis of breast cancer, improving the survival rate;
- allowing drugs to substitute for surgery -- drug therapy has been effective in allowing some patients with ulcers, gallstones, coronary artery disease, and hyperthyroidism to be treated without surgery; and
- improving the population's general health -- vaccines and new pharmaceuticals have virtually eliminated deaths in the US caused by polio and pertussis; smallpox has been eradicated from the face of the earth; the Hib vaccine is effective in preventing meningitis infections in children under age one (those with the highest infection rates); and the development of assays for detection of HIV antibodies in the sera of blood donors now routinely saves transfusion recipients from HIV infection.

Physicians have a responsibility to provide care, and we do not believe that our patients, the American people, will be willing to give up these advances. Instead of limits on expanding access to technology or decisions made on whether such advances should continue, we think that the focus should be on proper utilization of technology.

The development of practice parameters and aggressive technology assessment are the best means to curb inappropriate technology utilization. Practice parameters are strategies for patient management developed to help physicians make clinical decisions. Parameters help clarify appropriate utilization of technologies, resulting in better patient care. The AMA, with other medical societies, is directing the development and implementation of practice parameters. The AMA believes that one of the best ways to assure appropriate care is through further development, dissemination, and implementation of scientifically and clinically sound practice parameters/clinical guidelines by the medical profession itself.

Technology assessment studies the safety, effectiveness, indications for use, and cost effectiveness of technologies. The AMA's Diagnostic and Therapeutic Technology Assessment (DATTA) Program provides accurate information to physicians on the appropriate utilization of health care technology. DATTA evaluates the safety and effectiveness of drugs, devices, and procedures by integrating the expert opinions of physician-consultants with systematic reviews of the scientific literature.

As the health care debate begins to focus on allocating limited health care resources, the value of medical technology will become an increasingly important question. Expanded availability of medical technology greatly increases the number of treatment alternatives that physicians, patients, and their families will have available when they are needed. However, these decisions require value judgements that must include both clinical and nonclinical considerations along with patient preferences.

Our concern is that these preferences must be discussed and decisions must be made in the context of the patient/physician relationship. No limits should be placed on the medically appropriate technological choices available to them, but as much information as possible about those technologies should be developed to help them make the best judgements possible. Advances in health care technology and how that technology should be used must continue. Only then can true value, not just cost limitations, be achieved.

Sincerely,

James S. Todd MD

James S. Todd, MD

ATTACHMENT A

Health Care Technology

Health care technology is often cited as a factor contributing to the health care cost problem. Usually, the price of a new diagnostic device or the cost of a new procedure is cited as evidence. However, the impact of new technology on aggregate expenditures is not well understood. It also needs to be recognized that diffusion of new health care technology can reduce health care costs.

Diffusion of Medical Technology. New medical technologies diffuse rapidly through the U.S. health care sector.

- In 1980, only 20% of hospitals provided CT scanning services as compared with 61% in 1990.
- In 1980, 15% of hospitals provided cardiac catheterization services as compared with 24% in 1990.
- In 1980, 9% of hospitals provided open-heart surgery services as compared with 15% in 1990.
- In 1982, 3.5% of hospitals provided organ/tissue transplantation services as compared with 9% in 1990.[1]

Food and Drug Administration (FDA) Drug Approval Process

- Seven cents of the health care dollar can be attributed to drug costs--two cents for nonprescription and five cents for prescription drugs.
- Drug development is lengthy and increasingly expensive. A recent study by Joseph A. DiMasi, MD, of the Center for Drug Development at Tufts University places the average development time from chemical synthesis to approval for a new drug at 12 years, and at an estimated cost of $231 million in 1987 dollars.[2]

Beneficial Effects of New Medical Technology. Biomedical research has made substantial and lasting contributions to the improvement of the health and well-being of society.

- An individual born in the U.S. at the turn of the century faced an average life expectancy of 43 years as compared with over 70 years today.
- Over the past 20 years, deaths from childbirth have declined 72%, deaths from influenza and pneumonia have dropped 52%, and deaths from diabetes have fallen 31%. Deaths from heart disease and stroke have been declining since 1940, and the cure rate for all cancer patients has risen since 1971.[3,4]
- The polio vaccines developed by Salk and Sabin are responsible for dollar savings of approximately $2 billion (1960 dollars) annually.[5]

- Total cost reductions in medical care associated with the introduction and use of cimetidine, used in the treatment of duodenal ulcer, approximates $20 billion.[6]

- The discovery that lithium possessed a specific antimanic effect and the widespread application of this drug in psychiatry has saved a total of over $4 billion by restoring individuals with manic-depressive illness to productivity.[7]

- The Prospective Payment Assessment Commission has estimated that the use of extracorporeal shock wave lithotripsy will decrease Medicare costs associated with the treatment of kidney and ureteral stones by $16.2 million in 1991.[8]

Costs Increases Due to New Medical Technology. Increased intensity of services was an important factor accounting for growth in health care spending from 1985-1990. Increased intensity accounted for:

- 41.4% of the increase in the cost of inpatient services;

- 30.6% of the increase in the cost of outpatient services;

- 37.5% of the increase in the cost of physician services; and

- 32.6% of the increase in the cost of nursing home services.[1]

Setting of Care. Technological advances combined with changes in economic incentives in the reimbursement system have brought about shifts in site-of-service.

- Hospital admissions decreased by 6.6% form 1980-1985, and by 7.0% from 1985-1990.

- Outpatient visits increased by 7.3% from 1980-1985, and by 30.5% from 1985-1990.

- Physician visits increased by 18.8% from 1980-1985, and by 10.7% from 1985-1990.[1]

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